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=> d his ful

     FILE 'HCAPLUS' ENTERED AT 14:48:17 ON 24 JUL 2005
                  E MANGEL ALLEN WAYNE/AU
L19            49 SEA ABB=ON  ("MANGEL ALLEN W"/AU OR "MANGEL ALLEN WAYNE"/AU)
                  E NAYLOR ALAN/AU
L20            88 SEA ABB=ON  ("NAYLOR ALAN"/AU OR "NAYLOR ALAN ROBERT"/AU)
L21             2 SEA ABB=ON  L19 AND L20
                  SELECT RN L21 1-1

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L22            19 SEA ABB=ON  (123653-11-2/BI OR 158205-05-1/BI OR 162011-90-7/BI
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                  183610-65-3/BI OR 189954-66-3/BI OR 198470-84-7/BI OR 202409-33
                  -4/BI OR 220991-20-8/BI OR 221148-46-5/BI OR 267235-56-3/BI OR
                  342651-37-0/BI OR 51803-78-2/BI OR 80937-31-1/BI OR 329900-75-6
                  /BI OR 329967-85-3/BI OR 81098-60-4/BI)

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L24               ANALYZE L23 1 CT :       15 TERMS

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L26            11 SEA ABB=ON  (CELECOXIB OR ROFECOXIB OR VALDECOXIB OR PARECOXIB
                  OR COX 189 OR ETORICOXIB OR JTE-522 OR JTE522 OR DFP OR NS398
                  OR NS 398 OR L-745337 OR L745337)/CN
                  E JTE 522/CN
L27             1 SEA ABB=ON  "JTE 522"/CN
                  E NS-398
                  E NS 398/CN
L28             1 SEA ABB=ON  "NS 398"/CN
                  E L 745337/CN
L29             1 SEA ABB=ON  "L 745337"/CN
L30             0 SEA ABB=ON  L24
L31            13 SEA ABB=ON  L30 OR L26 OR L27 OR L28 OR L29

     FILE 'HCAPLUS' ENTERED AT 15:08:40 ON 24 JUL 2005
L32          7710 SEA ABB=ON  L31 OR (?CELECOXIB? OR ?ROFECOXIB? OR ?VALDECOXIB?
                  OR ?PARECOXIB? OR COX-189 OR COX 189 OR ?ETORICOXIB? OR MK663
                  OR MK 663 OR JTE522 OR JTE 522 OR DFP OR NS398 OR NS 398 OR
                  L745337 OR L 745337)
L33             0 SEA ABB=ON  L32 AND (NON?(W)?ULCER?(W)?DYSPEPSIA? OR ?INDIGESTI
                  ON?)
L34            30 SEA ABB=ON  L32 AND (?DYSPEPS? OR ?INDIGEST?)
L35             0 SEA ABB=ON  L34 AND GERD
L36             0 SEA ABB=ON  L34 AND ?GASTROESOPHAGEAL?(W)?REFLUX?(W)?DISEASE?
L37             1 SEA ABB=ON  L34 AND ?ESOPHAG?(W)?REFLUX?
L38            30 SEA ABB=ON  L34 OR L37
L39             5 SEA ABB=ON  L38 AND (PRD<20000201 OR PD<20000201)

     FILE 'USPATFULL' ENTERED AT 15:17:15 ON 24 JUL 2005
L40            14 SEA ABB=ON  L38 AND (PRD<20000201 OR PD<20000201)

     FILE 'MEDLINE, BIOSIS, EMBASE' ENTERED AT 15:18:01 ON 24 JUL 2005
L41            45 SEA ABB=ON  L39
L42            45 DUP REMOV L41 (0 DUPLICATES REMOVED)
L43             0 SEA ABB=ON  L42 AND ?GASTROESOPHAGEAL?(W) ?REFULX?(W) ?DISEASE?
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see blue tabs on Inventor Search for these 3 compds.

5 cits from CA Plus

4 cits from USPATFULL

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L44           0 SEA ABB=ON  L42 AND ?GASTROESOPHAGEAL?(W) ?REFLUX?(W) ?DISEASE?
L45          44 SEA ABB=ON  L42 AND ?HUMAN?
L46           0 SEA ABB=ON  L45 AND (NON?(W) ?ULCER?(W) ?DYSPEPSIA? OR
                ?INDIGEST?)
L47          44 SEA ABB=ON  L45 AND (?DYSPEPSIA? OR ?INDIGEST?)
L48           0 SEA ABB=ON  L47 AND NUD

     FILE 'HCAPLUS' ENTERED AT 15:24:29 ON 24 JUL 2005
L49           0 SEA ABB=ON  L34 AND NUD
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4/4 cits from above databases

FILE HCAPLUS

FILE COVERS 1907 - 24 Jul 2005 VOL 143 ISS 5
FILE LAST UPDATED: 22 Jul 2005 (20050722/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE MEDLINE
FILE LAST UPDATED: 23 JUL 2005 (20050723/UP). FILE COVERS 1950 TO DATE.

On December 19, 2004, the 2005 MeSH terms were loaded.

The MEDLINE reload for 2005 is now available. For details enter HELP RLOAD at an arrow promt (=>). See also:

http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html

OLDMEDLINE now back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2005 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE CANCERLIT
FILE COVERS 1963 TO 15 Nov 2002 (20021115/ED)

On July 28, 2002, CANCERLIT was reloaded. See HELP RLOAD for details.

CANCERLIT thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2002 vocabulary. Enter HELP THESAURUS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE BIOSIS
FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 21 July 2005 (20050721/ED)

FILE RELOADED: 19 October 2003.

FILE EMBASE
FILE COVERS 1974 TO 21 Jul 2005 (20050721/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE JAPIO
FILE LAST UPDATED: 4 JUL 2005 <20050704/UP>
FILE COVERS APR 1973 TO MARCH 31, 2005

<<< GRAPHIC IMAGES AVAILABLE >>>

FILE JICST-EPLUS
FILE COVERS 1985 TO 18 JUL 2005 (20050718/ED)

THE JICST-EPLUS FILE HAS BEEN RELOADED TO REFLECT THE 1999 CONTROLLED TERM (/CT) THESAURUS RELOAD.

FILE USPATFULL
FILE COVERS 1971 TO PATENT PUBLICATION DATE: 21 Jul 2005 (20050721/PD)
FILE LAST UPDATED: 21 Jul 2005 (20050721/ED)
HIGHEST GRANTED PATENT NUMBER: US6920641
HIGHEST APPLICATION PUBLICATION NUMBER: US2005160510
CA INDEXING IS CURRENT THROUGH 21 Jul 2005 (20050721/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 21 Jul 2005 (20050721/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Jun 2005
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Jun 2005

>>> USPAT2 is now available. USPATFULL contains full text of the <<<
>>> original, i.e., the earliest published granted patents or <<<
>>> applications. USPAT2 contains full text of the latest US <<<
>>> publications, starting in 2001, for the inventions covered in <<<
>>> USPATFULL. A USPATFULL record contains not only the original <<<
>>> published document but also a list of any subsequent <<<
>>> publications. The publication number, patent kind code, and <<<
>>> publication date for all the US publications for an invention <<<
>>> are displayed in the PI (Patent Information) field of USPATFULL <<<
>>> records and may be searched in standard search fields, e.g., /PN, <<<
>>> /PK, etc. <<<

>>> USPATFULL and USPAT2 can be accessed and searched together <<<
>>> through the new cluster USPATALL. Type FILE USPATALL to <<<
>>> enter this cluster. <<<
>>> <<<
>>> Use USPATALL when searching terms such as patent assignees, <<<
>>> classifications, or claims, that may potentially change from <<<
>>> the earliest to the latest publication. <<<

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE REGISTRY
Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 22 JUL 2005 HIGHEST RN 856698-04-9
DICTIONARY FILE UPDATES: 22 JUL 2005 HIGHEST RN 856698-04-9

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

****
* *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
* *
****

Structure search iteration limits have been increased. See HELP SLIMITS for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

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=> d que stat l39
L19          49 SEA FILE=HCAPLUS ABB=ON  ("MANGEL ALLEN W"/AU OR "MANGEL ALLEN
                WAYNE"/AU)
L20          88 SEA FILE=HCAPLUS ABB=ON  ("NAYLOR ALAN"/AU OR "NAYLOR ALAN
                ROBERT"/AU)
L21           2 SEA FILE=HCAPLUS ABB=ON  L19 AND L20
L22          19 SEA FILE=REGISTRY ABB=ON  (123653-11-2/BI OR 158205-05-1/BI OR
                162011-90-7/BI OR 169590-42-5/BI OR 180200-68-4/BI OR 181695-72
                -7/BI OR 183610-65-3/BI OR 189954-66-3/BI OR 198470-84-7/BI OR
                202409-33-4/BI OR 220991-20-8/BI OR 221148-46-5/BI OR 267235-56
                -3/BI OR 342651-37-0/BI OR 51803-78-2/BI OR 80937-31-1/BI OR
                329900-75-6/BI OR 329967-85-3/BI OR 81098-60-4/BI)
L23           2 SEA FILE=HCAPLUS ABB=ON  L21 AND L22
L24             ANALYZE  L23 1 CT :       15 TERMS
L26          11 SEA FILE=REGISTRY ABB=ON  (CELECOXIB OR ROFECOXIB OR VALDECOXIB
                 OR PARECOXIB OR COX 189 OR ETORICOXIB OR JTE-522 OR JTE522 OR
                DFP OR NS398 OR NS 398 OR L-745337 OR L745337)/CN
L27           1 SEA FILE=REGISTRY ABB=ON  "JTE 522"/CN
L28           1 SEA FILE=REGISTRY ABB=ON  "NS 398"/CN
L29           1 SEA FILE=REGISTRY ABB=ON  "L 745337"/CN
L30           0 SEA FILE=REGISTRY ABB=ON  L24
L31          13 SEA FILE=REGISTRY ABB=ON  L30 OR L26 OR L27 OR L28 OR L29
L32        7710 SEA FILE=HCAPLUS ABB=ON  L31 OR (?CELECOXIB? OR ?ROFECOXIB? OR
                ?VALDECOXIB? OR ?PARECOXIB? OR COX-189 OR COX 189 OR ?ETORICOXI
                B? OR MK663 OR MK 663 OR JTE522 OR JTE 522 OR DFP OR NS398 OR
                NS 398 OR L745337 OR L 745337)
L34          30 SEA FILE=HCAPLUS ABB=ON  L32 AND (?DYSPEPS? OR ?INDIGEST?)
L37           1 SEA FILE=HCAPLUS ABB=ON  L34 AND ?ESOPHAG?(W)?REFLUX?
L38          30 SEA FILE=HCAPLUS ABB=ON  L34 OR L37
L39           5 SEA FILE=HCAPLUS ABB=ON  L38 AND (PRD<20000201 OR PD<20000201)

=> d ibib abs l39 1-5

L39  ANSWER 1 OF 5  HCAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2000:806202  HCAPLUS
DOCUMENT NUMBER:          135:280
TITLE:                    Gastrointestinal tolerability of the selective
                          cyclooxygenase-2 (COX-2) inhibitor rofecoxib
                          compared with nonselective COX-1 and COX-2 inhibitors
                          in osteoarthritis
AUTHOR(S):                Watson, Douglas J.; Harper, Sean E.; Zhao, Peng-Liang;
                          Quan, Hui; Bolognese, James A.; Simon, Thomas J.
CORPORATE SOURCE:         Merck Research Laboratories, West Point, PA, USA
SOURCE:                   Archives of Internal Medicine (2000),
                          160(19), 2998-3003
                          CODEN: AIMDAP; ISSN: 0003-9926
PUBLISHER:                American Medical Association
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   Most nonsteroidal anti-inflammatory drugs (NSAIDs) are nonselective
     cyclooxygenase (COX-1 and CON-2) inhibitors and are associated with a variety
     of upper gastrointestinal (GI) tract symptoms.  The roles of COX-1 and
     COX-2 in the pathogenesis of these symptoms are unclear.  To test whether
     COX-2 inhibition with rofecoxib would have greater GI
     tolerability than nonselective COX-1 and COX-2 inhibition, we compared the
     incidences of (1) treatment discontinuations for GI adverse events (AEs)
     and (2) prespecified dyspeptic-type GI AEs among patients with
     osteoarthritis treated with rofecoxib vs. NSAIDs.  A
     prespecified, combined anal. of investigator-reported GI AEs in all 8
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double-blind, randomized, phase 2b/3 osteoarthritis trials of **rofecoxib** was conducted. Patients included men and women with osteoarthritis (N = 5435); there was no upper age limit for entry. Treatments tested included **rofecoxib**, 12.5, 25, or 50 mg (combined), vs. ibuprofen, diclofenac, or nabumetone (combined). Primary outcomes were the time (by survival anal.) to (1) treatment discontinuation due to GI AEs and (2) first reported dyspeptic-type GI AE. Between-treatment comparisons were made by log-rank test. The number of treatment discontinuations caused by GI AEs during 12 mo was significantly lower (P=.02) with **rofecoxib** vs. NSAIDs (8.2 vs. 12.0 per 100 patient-years; relative risk, 0.70; 95% confidence interval, 0.52-0.94). The incidence of prespecified dyspeptic-type GI AEs during the first 6 mo was significantly lower (P=.02) with **rofecoxib** vs. NSAIDs (69.3 vs. 85.2 per 100 patient-years; relative risk, 0.85; 95% confidence interval, 0.74-0.97). However, the difference between treatments in dyspeptic-type GI AEs was attenuated after 6 mo. **Rofecoxib** was associated with a lower incidence of treatment discontinuations due to GI AEs over 12 mo and a lower incidence of dyspeptic-type GI AEs over 6 mo than treatment with nonselective COX inhibitors, or NSAIDs.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L39 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:593639 HCAPLUS
DOCUMENT NUMBER: 134:95253
TITLE: Upper gastrointestinal tolerability of **celecoxib**, a COX-2 specific inhibitor, compared to naproxen and placebo
AUTHOR(S): Bensen, William G.; Zhao, Sean Z.; Burke, Thomas A.; Zabinski, Richard A.; Makuch, Robert W.; Maurath, Clement J.; Agrawal, Naurang M.; Geis, G. Steven
CORPORATE SOURCE: Global Health Outcomes Statistics, Clinical Research, Pharmacia, Skokie, IL, 60077, USA
SOURCE: Journal of Rheumatology (**2000**), 27(8), 1876-1883
CODEN: JRHUA9; ISSN: 0315-162X
PUBLISHER: Journal of Rheumatology Publishing Co. Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The upper gastrointestinal (GI) tolerability of **celecoxib**, naproxen, and placebo was determined in patients with rheumatoid arthritis (RA) and osteoarthritis (OA). An anal. of 5, 12-wk, randomized, double blind, parallel group, placebo controlled clin. trials was conducted. In these trials, patients were randomized to: naproxen 500 mg bid (n = 1099), placebo (n = 1136), **celecoxib** 50 mg bid (n = 690) (subtherapeutic dose), **celecoxib** 100 mg (n = 1131) or 200 mg bid (n = 1125) (therapeutic dose), or **celecoxib** 400 mg bid (n = 434) (supra-therapeutic dosage). The incidence and time until moderate to severe abdominal pain, **dyspepsia**, nausea, and any of the aforementioned 3 upper GI symptoms (composite endpoint) were determined using time-to-event anal. The cumulative incidences of moderate to severe abdominal pain, **dyspepsia**, or nausea (composite endpoint) were: naproxen 500 mg (12.0%; 95% CI 9.9%-14.0%), **celecoxib** 50 mg bid (7.1%; 95% CI 5.0%-9.2%), **celecoxib** 100 mg bid (7.8%; 95% CI 6.0%-9.5%), **celecoxib** 200 mg bid (8.1%; 95% CI 6.4%-9.9%), **celecoxib** 400 mg bid (6.0%; 95% CI 3.6%-8.4%), and placebo (8.5%; 95% CI 6.5%-10.8%). After controlling for independent predictors of the composite endpoint, relative risks (RR) for the various treatments relative to naproxen 500 mg bid were: **celecoxib** 50 mg (RR 0.54;

95% CI 0.37-0.77; p < 0.001), **celecoxib** 100 mg (RR 0.60; 95% CI 0.45-0.80; p <0.001), **celecoxib** 200 mg bid (RR 0.63; 95% CI 0.47-0.83; p=0.001), **celecoxib** 400 mg bid (RR 0.56; 95% CI 0.35-0.89; p = 0.015), and placebo (RR 0.63; 95% CI 0.47-0.85; p = 0.002). After controlling for independent predictors of the composite endpoint, **celecoxib** treatment group patients did not differ from placebo patients when reporting the composite endpoint, with p values ranging from 0.40 to 0.96. The upper GI tolerability of **celecoxib** is superior to naproxen. A dose-response relationship between **celecoxib** and upper GI symptoms was not apparent..

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L39 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:476259 HCAPLUS
TITLE: Inhibitors of cyclooxygenase-2: November 1999 - April 2000
AUTHOR(S): Carter, Jeffery S.
CORPORATE SOURCE: Pharmacia Corp., St Louis, MO, 63198, USA
SOURCE: Expert Opinion on Therapeutic Patents (**2000**), 10(7), 1011-1020
CODEN: EOTPEG; ISSN: 1354-3776
PUBLISHER: Ashley Publications Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Since the discovery of aspirin, the search for safer and more efficacious agents for the treatment of inflammation, pain and fever has continued for more than a century. Agents such as aspirin, the first synthetic NSAID, exert their effect by inhibiting the conversion of arachidonic acid to prostaglandins via the cyclooxygenase (COX) enzyme pathway. Beyond their therapeutic utility, traditional NSAIDs possess predictable side effects including **dyspepsia**, GI ulceration and antiplatelet activity. It is now well established that two isoforms of COX exist. COX-1 is constitutively formed and is responsible for production of basal levels of prostaglandins needed for GI tract homeostasis, proper renal filtration rate and platelet aggregatory function. Biosynthesis of the COX-2 enzyme is induced by pro-inflammatory stimuli such as IL-1, TNF-α, growth factors and endotoxin LPS. The elevated levels of prostaglandins produced by the newly formed COX-2 cause the pathol. symptoms of inflammation. Favorably, specific COX-2 inhibitors display efficacy as analgesic and anti-inflammatory agents without causing GI damage and antiplatelet activity demonstrated by traditional, non-selective NSAIDs. The decreased GI side effect profile may explain the rapid acceptance of the first two COX-2 inhibitors marketed, **celecoxib** and **rofecoxib**, which garnered over US$2 billion from their combined partial year of sales in 1999. COX-2 specific agents, due to their higher therapeutic index, can be studied at levels in excess of their therapeutic, anti-inflammatory dosage. Consequently, many new areas of research have become available. Pivotal preclin. and clin. research in the chemoprevention and treatment of cancer and the treatment of Alzheimer's disease is in progress. This review will cover the recent patent literature (Nov. 1999 - Apr. 2000) including new chemical classes and new filings on previously disclosed series.

REFERENCE COUNT: 75 THERE ARE 75 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L39 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:308911 HCAPLUS
DOCUMENT NUMBER: 132:317550

TITLE: Meloxicam: a COX-2-specific NSAID for the treatment of osteoarthritis
AUTHOR(S): Siepler, John K.
CORPORATE SOURCE: Department of pharmaceutical services, school of pharmacy, University of California at Davis Medical Center, University of California at San Francisco, USA
SOURCE: Formulary (**2000**), 35(4), 317-320,322,327
CODEN: FORMF9; ISSN: 1082-801X
PUBLISHER: Advanstar Communications, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 26 refs. Meloxicam is a COX-2-specific nonsteroidal anti-inflammatory drug (NSAID) under FDA review for the treatment of osteoarthritis. In vitro studies demonstrate that it has greater COX-2 selectivity than traditional NSAIDs, such as naproxen, but less than the COX-2-specific agents **celecoxib** or **rofecoxib.** In comparative trials in patients with osteoarthritis and rheumatoid arthritis, meloxicam has generally demonstrated similar efficacy to naproxen, diclofenac, and piroxicam. Gastrointestinal adverse reactions appear to be less frequent with meloxicam than with traditional non-COX-2-specific NSAIDs. In two large trials, patients receiving meloxicam experienced significantly less **dyspepsia**, nausea, vomiting, and abdominal pain than those receiving piroxicam or diclofenac. Studies have not yet demonstrated whether the incidence of perforations, ulcerations, and gastrointestinal bleeding is lower with meloxicam than with other NSAIDs. Studies comparing meloxicam with **celecoxib** or **rofecoxib** have not yet been conducted.
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L39 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:72484 HCAPLUS
DOCUMENT NUMBER: 132:87911
TITLE: **Celecoxib** versus diclofenac in long-term management of rheumatoid arthritis: randomized double-blind comparison
AUTHOR(S): Emery, Paul; Zeidler, Henning; Kvien, Tore K.; Guslandi, Mario; Naudin, Raphael; Stead, Helen; Verburg, Kenneth M.; Isakson, Peter C.; Hubbard, Richard C.; Geis, G. Steven
CORPORATE SOURCE: Department of Rheumatology and Rehabilltation, University of Leeds, Leeds, UK
SOURCE: Lancet (**1999**), 354(9196), 2106-2111
CODEN: LANCAO; ISSN: 0140-6736
PUBLISHER: Lancet Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Background: Non-steroidal anti-inflammatory drugs (NSAIDs) inhibit cyclo-oxygenase (COX), which leads to suppression of COX-1-mediated production of gastrointestinal-protective prostaglandins. Gastrointestinal injury is a common outcome. We compared the efficacy, safety, and tolerability of long-term therapy with **celecoxib**, a COX-1 sparing inhibitor of COX-2, with diclofenac, a non-specific COX inhibitor. Methods: 655 patients with adult-onset rheumatoid arthritis of at least 6 mo' duration were randomly assigned oral **celecoxib** 200 mg twice daily or diclofenac SR 75 mg twice daily for 24 wk. Anti-inflammatory and analgesic activity and tolerability were assessed at baseline, every 4 wk, and at week 24. We assessed gastrointestinal safety by upper-gastrointestinal endoscopy within 7 days of the last treatment dose

at centers where the procedure was available. Anal. was by intention-to-treat. Findings: 430 patients underwent endoscopy (**celecoxib** n=212, diclofenac n=218). The two drugs were similar in management of rheumatoid arthritis pain and inflammation. Gastroduodenal ulcers were detected endoscopically in 33 (15%) patients treated with diclofenac and in eight (4%) in the **celecoxib** group (p<0.001). The rate of withdrawal for any gastrointestinal-related adverse event, most commonly abdominal pain, diarrhea, and **dyspepsia**, was nearly three times higher in the diclofenac-treated group than in the **celecoxib** group (16 vs. 6%; p<0.001). Interpretation: **Celecoxib** showed sustained anti-inflammatory and analgesic activity similar to diclofenac, with a lower frequency of upper gastrointestinal ulceration or gastrointestinal adverse events, and tolerability was better.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> d que stat l40
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L20          88 SEA FILE=HCAPLUS ABB=ON  ("NAYLOR ALAN"/AU OR "NAYLOR ALAN
                ROBERT"/AU)
L21           2 SEA FILE=HCAPLUS ABB=ON  L19 AND L20
L22          19 SEA FILE=REGISTRY ABB=ON  (123653-11-2/BI OR 158205-05-1/BI OR
                162011-90-7/BI OR 169590-42-5/BI OR 180200-68-4/BI OR 181695-72
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                202409-33-4/BI OR 220991-20-8/BI OR 221148-46-5/BI OR 267235-56
                -3/BI OR 342651-37-0/BI OR 51803-78-2/BI OR 80937-31-1/BI OR
                329900-75-6/BI OR 329967-85-3/BI OR 81098-60-4/BI)
L23           2 SEA FILE=HCAPLUS ABB=ON  L21 AND L22
L24             ANALYZE  L23 1 CT :      15 TERMS
L26          11 SEA FILE=REGISTRY ABB=ON  (CELECOXIB OR ROFECOXIB OR VALDECOXIB
                 OR PARECOXIB OR COX 189 OR ETORICOXIB OR JTE-522 OR JTE522 OR
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L28           1 SEA FILE=REGISTRY ABB=ON  "NS 398"/CN
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L30           0 SEA FILE=REGISTRY ABB=ON  L24
L31          13 SEA FILE=REGISTRY ABB=ON  L30 OR L26 OR L27 OR L28 OR L29
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                B? OR MK663 OR MK 663 OR JTE522 OR JTE 522 OR DFP OR NS398 OR
                NS 398 OR L745337 OR L 745337)
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L37           1 SEA FILE=HCAPLUS ABB=ON  L34 AND ?ESOPHAG?(W)?REFLUX?
L38          30 SEA FILE=HCAPLUS ABB=ON  L34 OR L37
L40          14 SEA FILE=USPATFULL ABB=ON  L38 AND (PRD<20000201 OR PD<20000201
                )

=> d ibib abs l40 1-14

L40  ANSWER 1 OF 14  USPATFULL on STN
ACCESSION NUMBER:         2005:183025  USPATFULL
TITLE:                    Dried forms of aqueous solubilized bile acid dosage
                          formulation: preparation and uses thereof
INVENTOR(S):              Yoo, Seo Hong, Wyckoff, NJ, UNITED STATES

                               NUMBER        KIND    DATE
                          ---------------- ------ --------
PATENT INFORMATION:       US 2005158408      A1   20050721
APPLICATION INFO.:        US 2004-996945     A1   20041124  (10)
RELATED APPLN. INFO.:     Continuation-in-part of Ser. No. US 2001-778154, filed
                          on 5 Feb 2001, PENDING Continuation-in-part of Ser. No.
                          US 1999-357549, filed on 20 Jul 1999, GRANTED, Pat. No.
                          US 6251428

                                 NUMBER         DATE
                          ------------------ --------
PRIORITY INFORMATION:     US 1998-94069P     19980724 (60)          <--
DOCUMENT TYPE:            Utility
FILE SEGMENT:             APPLICATION
LEGAL REPRESENTATIVE:     BAKER & BOTTS, 30 ROCKEFELLER PLAZA, NEW YORK, NY,
                          10112, US
NUMBER OF CLAIMS:         42
EXEMPLARY CLAIM:          1
NUMBER OF DRAWINGS:       15 Drawing Page(s)
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LINE COUNT: 2133

AB Compositions for pharmaceutical and other uses comprising clear aqueous solutions of bile acids which do not form any detectable precipitates over selected ranges of pH values of the aqueous solution and methods of making such solutions are disclosed. Compositions of the disclosure may comprise water; a bile acid in the form of a bile acid, bile acid salt, or a bile acid conjugated with an amine by an amide linkage; and either or both an aqueous soluble starch conversion product and an aqueous soluble non-starch polysaccharide. The composition remains in solution without forming a precipitate over a range of all pH values obtainable in an aqueous system. The composition, according to some embodiments, may further contain a pharmaceutical compound in a pharmaceutically effective amount. The disclosure further provides dried forms of primary aqueous solubilized bile acid formulations and methods of preparing such dried forms.

L40 ANSWER 2 OF 14 USPATFULL on STN

ACCESSION NUMBER: 2004:58076 USPATFULL

TITLE: Exo-S-mecamylamine formulation and use in treatment

INVENTOR(S): Shytle, Douglas, Lutz, FL, UNITED STATES
Sanberg, Paul, Spring Hills, FL, UNITED STATES
Newman, Mary, Valrico, FL, UNITED STATES
Silver, Archie A., Tampa, FL, UNITED STATES

PATENT ASSIGNEE(S): University of South Florida (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004044083	A1	20040304
APPLICATION INFO.:	US 2003-441947	A1	20030923 (10)

RELATED APPLN. INFO.: Continuation of Ser. No. US 2001-882935, filed on 15 Jun 2001, PENDING Continuation-in-part of Ser. No. WO 1999-US30153, filed on 16 Dec 1999, PENDING

	NUMBER	DATE	
PRIORITY INFORMATION:	US 1998-112534P	19981216 (60)	<--

DOCUMENT TYPE: Utility

FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: Carl B. Massey, Jr., Womble Carlyle Sandridge & Rice, PLLC, Post Office Box 7037, Atlanta, GA, 30357-0037

NUMBER OF CLAIMS: 20

EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 5 Drawing Page(s)

LINE COUNT: 1443

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A pharmaceutical composition includes a therapeutically effective amount of exo-S-mecamylamine or a pharmaceutically acceptable salt thereof, substantially free of exo-R-mecamylamine in combination with a pharmaceutically acceptable carrier. Preferably the amount is about 0.5 mg to about 20 mg. Medical conditions are treated by administering a therapeutically effective amount of exo-S-mecamylamine or a pharmaceutically acceptable salt thereof, substantially free of its exo-R-mecamylamine, said amount being sufficient to ameliorate the medical condition. The medical conditions include but are not limited to substance addiction (involving nicotine, cocaine, alcohol, amphetamine, opiate, other psychostimulant and a combination thereof), aiding smoking cessation, treating weight gain associated with smoking cessation, hypertension, hypertensive crisis, Tourette's Syndrome and other

tremors, cancer (such as small cell lung cancer), atherogenic profile, neuropsychiatric disorders (such as bipolar disorder, depressoin, an anxiety disorder, schizophrenia, a seizure disorder, Parkinson's disease and attention deficit hyperactivity disorder), chronic fatigue syndrome, Crohn's disease, autonomic dysreflexia, and spasmogenic intestinal disorders.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L40 ANSWER 3 OF 14 USPATFULL on STN
ACCESSION NUMBER: 2004:4504 USPATFULL
TITLE: Tumor necrosis factor receptor 2
INVENTOR(S): Stanton, Jr., Vincent P., Belmont, MA, United States
PATENT ASSIGNEE(S): Nuvelo, Inc., Sunnyvale, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6673908	B1	20040106
APPLICATION INFO.:	US 2001-968455		20011001 (9)

RELATED APPLN. INFO.: Division of Ser. No. US 2000-649035, filed on 25 Aug 2000 Continuation-in-part of Ser. No. US 2000-590749, filed on 8 Jun 2000, now abandoned Continuation-in-part of Ser. No. US 2000-495780, filed on 1 Feb 2000, now abandoned Continuation-in-part of Ser. No. US 2000-492712, filed on 27 Jan 2000, now abandoned Continuation-in-part of Ser. No. WO 2000-US1392, filed on 20 Jan 2000 Continuation-in-part of Ser. No. US 968455 Continuation-in-part of Ser. No. US 1999-451252, filed on 29 Nov 1999, now abandoned Continuation-in-part of Ser. No. US 1999-427835, filed on 26 Oct 1999, now abandoned Continuation-in-part of Ser. No. US 1999-414330, filed on 6 Oct 1999, now abandoned Continuation-in-part of Ser. No. US 1999-389993, filed on 3 Sep 1999, now abandoned Continuation-in-part of Ser. No. US 1999-370841, filed on 9 Aug 1999, now abandoned Continuation-in-part of Ser. No. US 1999-300747, filed on 26 Apr 1999, now abandoned

	NUMBER	DATE	
PRIORITY INFORMATION:	US 1999-131334P	19990426 (60)	<--
	US 1999-131191P	19990426 (60)	<--
	US 1999-121047P	19990222 (60)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Benzion, Gary
ASSISTANT EXAMINER: Chakrabarti, Arun Kr.
LEGAL REPRESENTATIVE: Fish & Richardson P.C.
NUMBER OF CLAIMS: 10
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 0 Drawing Figure(s); 0 Drawing Page(s)
LINE COUNT: 17463
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present disclosure describes the use of genetic variance information for genes involved in inflammatory or immunologic disease, disorder, or dysfunction. The variance information is indicative of the expected response of a patient to a method of treatment. Methods of determining

relevant variance information and additional methods of using such variance information are also described.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L40 ANSWER 4 OF 14 USPATFULL on STN

ACCESSION NUMBER:	2003:312624 USPATFULL
TITLE:	Nitrosated and nitrosylated cyclooxygenase-2 inhibitors, compositions and methods of use
INVENTOR(S):	Bandarage, Ramani R., Newton, MA, UNITED STATES Bandarage, Upul K., Newton, MA, UNITED STATES Fang, Xinqin, Lexington, MA, UNITED STATES Garvey, David S., Dover, MA, UNITED STATES Letts, L. Gordon, Dover, MA, UNITED STATES Schroeder, Joseph D., Dedham, MA, UNITED STATES Tam, Sang William, Dover, MA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003220228	A1	20031127
APPLICATION INFO.:	US 2003-463671	A1	20030618 (10)

RELATED APPLN. INFO.: Division of Ser. No. US 2000-741816, filed on 22 Dec 2000, PENDING

	NUMBER	DATE	
PRIORITY INFORMATION:	US 1999-171623P	19991223 (60)	<--
	US 2000-226085P	20000818 (60)	

DOCUMENT TYPE:	Utility
FILE SEGMENT:	APPLICATION
LEGAL REPRESENTATIVE:	EDWARD D GRIEFF, HALE & DORR LLP, 1455 PENNSYLVANIA AVE, NW, WASHINGTON, DC, 20004
NUMBER OF CLAIMS:	58
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	5 Drawing Page(s)
LINE COUNT:	5947

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention describes novel nitrosated and/or nitrosylated cyclooxygenase 2 (COX-2) inhibitors and novel compositions comprising at least one nitrosated and/or nitrosylated cyclooxygenase 2 (COX-2) inhibitor, and, optionally, at least one compound that donates, transfers or releases nitric oxide, stimulates endogenous synthesis of nitric oxide, elevates endogenous levels of endothelium-derived relaxing factor or is a substrate for nitric oxide synthase, and/or optionally, at least one therapeutic agent, such as, steroids, nonsteroidal antiinflammatory compounds (NSAID), 5-lipoxygenase (5-LO) inhibitors, leukotriene B.sub.4 (LTB.sub.4) receptor antagonists, leukotriene A.sub.4 (LTA.sub.4) hydrolase inhibitors, 5-HT agonists, 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) inhibitors, H.sub.2antagonists, antineoplastic agents, antiplatelet agents, decongestants, diuretics, sedating or non-sedating anti-histamines, inducible nitric oxide synthase inhibitors, opioids, analgesics, Helicobacter pylori inhibitors, proton pump inhibitors, isoprostane inhibitors, and mixtures thereof. The present invention also provides novel compositions comprising at least one parent COX-2 inhibitor and at least one nitric oxide donor, and, optionally, at least one therapeutic agent. The present invention also provides kits and methods for treating inflammation, pain and fever; for treating and/or improving the gastrointestinal properties of COX-2 inhibitors; for facilitating wound

healing; for treating and/or preventing renal toxicity; and for treating and/or preventing other disorders resulting from elevated levels of cyclooxygenase-2.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L40 ANSWER 5 OF 14 USPATFULL on STN

ACCESSION NUMBER:	2003:254992 USPATFULL
TITLE:	Method for cancer pain treatment
INVENTOR(S):	Du Pen, Stuart L., Bainbridge Island, WA, UNITED STATES Du Pen, Anna R., Bainbridge Island, WA, UNITED STATES
PATENT ASSIGNEE(S):	Du Pen, Inc., Bainbridge Island, WA (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003178031	A1	20030925
APPLICATION INFO.:	US 2002-268179	A1	20021009 (10)

RELATED APPLN. INFO.: Continuation of Ser. No. US 2000-565644, filed on 5 May 2000, ABANDONED

	NUMBER	DATE	
PRIORITY INFORMATION:	US 1999-133044P	19990507 (60)	<--

DOCUMENT TYPE:	Utility
FILE SEGMENT:	APPLICATION
LEGAL REPRESENTATIVE:	SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVE, SUITE 6300, SEATTLE, WA, 98104-7092
NUMBER OF CLAIMS:	4
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	43 Drawing Page(s)
LINE COUNT:	4624

AB A patient pain management system and method that includes assessing patient history; determining a drug treatment in response to assessing patient history; and repeatedly reassessing the pain and assessing side-effects and adjusting the drug treatment to minimize patient pain. The system includes pain assessment tools for assessing patient pain and treatment history; treatment choice tools for determining a pain treatment protocol; pain reassessment tools for reassessing patient pain in response to the pain treatment protocol; and side-effect assessment tools for assessing side-effects experienced by the patient to enable a caregiver to continuously reassess patient pain and comfort and adjust treatment to minimize patient pain and discomfort.

L40 ANSWER 6 OF 14 USPATFULL on STN

ACCESSION NUMBER:	2003:148995 USPATFULL
TITLE:	DFMO and **celecoxib** in combination for cancer chemoprevention and therapy
INVENTOR(S):	Love, Richard, San Antonio, TX, United States
PATENT ASSIGNEE(S):	ILEX Oncology, Inc., San Antonio, TX, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6573290	B1	20030603
APPLICATION INFO.:	US 2000-573089		20000517 (9)

	NUMBER	DATE

PRIORITY INFORMATION: US 1999-134582P 19990517 (60) <--
DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Goldberg, Jerome D.
LEGAL REPRESENTATIVE: Fulbright & Jaworski L.L.P.
NUMBER OF CLAIMS: 24
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 4 Drawing Figure(s); 3 Drawing Page(s)
LINE COUNT: 1330
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB **Celecoxib**, a COX-2 specific non-steroidal anti-inflammatory agent, is provided in combination with DFMO for the prevention and/or treatment of cancers. Provided with the present invention are pharmaceutically acceptable compositions that include a non-steroidal anti-inflammatory agent, **celecoxib**, together with an effective amount of difluoromethylornithine.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L40 ANSWER 7 OF 14 USPATFULL on STN
ACCESSION NUMBER: 2003:57971 USPATFULL
TITLE: Treatment of migraine headache
INVENTOR(S): Plachetka, John R., Chapel Hill, NC, UNITED STATES
Chowhan, Zakauddin T., Gaithersburg, MD, UNITED STATES
PATENT ASSIGNEE(S): POZEN Inc. (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003040537	A1	20030227
APPLICATION INFO.:	US 2002-255036	A1	20020926 (10)

RELATED APPLN. INFO.: Division of Ser. No. US 2000-517751, filed on 3 Mar 2000, GRANTED, Pat. No. US 6479551 Continuation-in-part of Ser. No. US 1997-966506, filed on 10 Nov 1997, GRANTED, Pat. No. US 6077539 Continuation-in-part of Ser. No. US 1996-748332, filed on 12 Nov 1996, ABANDONED

	NUMBER	DATE
PRIORITY INFORMATION:	WO 1997-US20611	19971112 <--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: FITCH, EVEN, TABIN & FLANNERY, SUITE 401L, 1801 K STREET, NW, WASHINGTON, DC, 20006-1201
NUMBER OF CLAIMS: 66
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 5 Drawing Page(s)
LINE COUNT: 1222
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention is directed to pharmaceutical compositions useful in the treatment of migraine. The compositions contain metoclopramide and one or more NSAIDs in unit dosage form. By selecting NSAIDs that are non-acidic or segregating the metoclopramide and NSAID, the storage life of the compositions has been increased. Also disclosed are coordinated dosage forms for the sequential release of drugs. The invention encompasses methods of treating migraine using any of these dosage forms.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L40 ANSWER 8 OF 14 USPATFULL on STN
ACCESSION NUMBER: 2003:4089 USPATFULL
TITLE: Formulatios of adenosine a1 agonists
INVENTOR(S): Bountra, Charanjit, Stevenage, UNITED KINGDOM
Clayton, Nicholas Maughan, Stevenage, UNITED KINGDOM
Naylor, Alan, Stevenage, UNITED KINGDOM

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2003004128	A1	20030102	
APPLICATION INFO.:	US 2002-168195	A1	20020618	(10)
	WO 2000-GB4883		20001219	

	NUMBER	DATE	
PRIORITY INFORMATION:	GB 1999-30075	19991220	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: DAVID J LEVY, CORPORATE INTELLECTUAL PROPERTY, GLAXOSMITHKLINE, FIVE MOORE DR., PO BOX 13398, RESEARCH TRIANGLE PARK, NC, 27709-3398
NUMBER OF CLAIMS: 14
EXEMPLARY CLAIM: 1
LINE COUNT: 895
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides a method of treating conditions associated with pain and alleviating the symptoms associated therewith which comprises administering to a mammal, including man, an adenosine A1 agonist or a physiologically acceptable salt or solvate thereof and an NSAID, e.g. a COX-2 inhibitor, or a physiologically acceptable salt or solvate thereof. The present invention also provides pharmaceutical formulations and patient packs comprising said combinations.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L40 ANSWER 9 OF 14 USPATFULL on STN
ACCESSION NUMBER: 2002:297630 USPATFULL
TITLE: Treatment of migraine headache
INVENTOR(S): Plachetka, John R., Chapel Hill, NC, United States
Chowhan, Zakauddin T., Gaithersburg, MD, United States
PATENT ASSIGNEE(S): Pozen Inc., Chapel Hill, NC, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6479551	B1	20021112	
APPLICATION INFO.:	US 2000-517751		20000303	(9)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1997-966506, filed on 10 Nov 1997, now patented, Pat. No. US 6077539 Continuation-in-part of Ser. No. US 1996-748332, filed on 12 Nov 1996, now abandoned			

	NUMBER	DATE	
PRIORITY INFORMATION:	WO 1997-US20611	19971112	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Dees, Jose G.

ASSISTANT EXAMINER: Choi, Frank
LEGAL REPRESENTATIVE: Sanzo, Michael A., Fitch, Even, Tabin & Flannery
NUMBER OF CLAIMS: 41
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 7 Drawing Figure(s); 5 Drawing Page(s)
LINE COUNT: 1326
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention is directed to pharmaceutical compositions useful in the treatment of migraine. The compositions contain metoclopramide and one or more NSAIDs in unit dosage form. By selecting NSAIDs that are non-acidic or segregating the metoclopramide and NSAID, the storage life of the compositions has been increased. Also disclosed are coordinated dosage forms for the sequential release of drugs. The invention encompasses methods of treating migraine using any of these dosage forms.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L40 ANSWER 10 OF 14 USPATFULL on STN
ACCESSION NUMBER: 2002:27523 USPATFULL
TITLE: Exo-S-mecamylamine formulation and use in treatment
INVENTOR(S): Shytle, Douglas, Lutz, FL, UNITED STATES
Sanberg, Paul, Spring Hill, FL, UNITED STATES
Newman, Mary, Valrico, FL, UNITED STATES
Silver, Archie A., Tampa, FL, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002016371	A1	20020207
	US 6734215	B2	20040511
APPLICATION INFO.:	US 2001-882935	A1	20010615 (9)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. WO 1999-US30153, filed on 16 Dec 1999, UNKNOWN

	NUMBER	DATE	
PRIORITY INFORMATION:	US 1998-112534P	19981216 (60)	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Barbara J. Luther, Chartered, 18124 Wedge Parkway, PMB 516, Reno, NV, 89511
NUMBER OF CLAIMS: 20
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 5 Drawing Page(s)
LINE COUNT: 1445
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A pharmaceutical composition includes a therapeutically effective amount of exo-S-mecamylamine or a pharmaceutically acceptable salt thereof, substantially free of exo-R-mecamylamine in combination with a pharmaceutically acceptable carrier. Preferably the amount is about 0.5 mg to about 20 mg. Medical conditions are treated by administering a therapeutically effective amount of exo-S-mecamylamine or a pharmaceutically acceptable salt thereof, substantially free of its exo-R-mecamylamine, said amount being sufficient to ameliorate the medical condition. The medical conditions include but are not limited to substance addiction (involving nicotine, cocaine, alcohol, amphetamine, opiate, other psychostimulant and a combination thereof), aiding smoking cessation, treating weight gain associated with smoking cessation, hypertension, hypertensive crisis, Tourette's Syndrome and other

tremors, cancer (such as small cell lung cancer), atherogenic profile, neuropsychiatric disorders (such as bipolar disorder, depression, an anxiety disorder, schizophrenia, a seizure disorder, Parkinson's disease and attention deficit hyperactivity disorder), chronic fatigue syndrome, Crohn's disease, autonomic dysreflexia, and spasmogenic intestinal disorders.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L40 ANSWER 11 OF 14 USPATFULL on STN

ACCESSION NUMBER:	2002:27522 USPATFULL		
TITLE:	Exo-R-mecamylamine formulation and use in treatment		
INVENTOR(S):	Shytle, Douglas, Lutz, FL, UNITED STATES Sanberg, Paul, Spring Hill, FL, UNITED STATES Newman, Mary, Valrico, FL, UNITED STATES Silver, Archie A., Tampa, FL, UNITED STATES		
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002016370	A1	20020207
APPLICATION INFO.:	US 2001-882934	A1	20010615 (9)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. WO 1999-US30137, filed on 16 Dec 1999, UNKNOWN		
	NUMBER	DATE	
PRIORITY INFORMATION:	US 1998-112534P	19981216 (60)	<--
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	APPLICATION		
LEGAL REPRESENTATIVE:	Barbara J. Luther, Chartered, 18124 Wedge Parkway, PMB 516, Reno, NV, 89511		
NUMBER OF CLAIMS:	20		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	5 Drawing Page(s)		
LINE COUNT:	1453		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A pharmaceutical composition includes a therapeutically effective amount of exo-R-mecamylamine or a pharmaceutically acceptable salt thereof, substantially free of exo-S-mecamylamine in combination with a pharmaceutically acceptable carrier. Preferably the amount is about 0.5 mg to about 20 mg. Medical conditions are treated by administering a therapeutically effective amount of exo-R-mecamylamine or a pharmaceutically acceptable salt thereof, substantially free of its exo-S-mecamylamine, said amount being sufficient to ameliorate the medical condition. The medical conditions include but are not limited to substance addiction (involving nicotine, cocaine, alcohol, amphetamine, opiate, other psychostimulant and a combination thereof), aiding smoking cessation, treating weight gain associated with smoking cessation, hypertension, hypertensive crisis, Tourette's Syndrome and other tremors, cancer (such as small cell lung cancer), atherogenic profile, neuropsychiatric disorders (such as bipolar disorder, depression, an anxiety disorder, schizophrenia, a seizure disorder, Parkinson's disease and attention deficit hyperactivity disorder), chronic fatigue syndrome, Crohn's disease, autonomic dysreflexia, and spasmogenic intestinal disorders.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L40 ANSWER 12 OF 14 USPATFULL on STN

ACCESSION NUMBER: 2001:205933 USPATFULL
TITLE: Nitrosated and nitrosylated cyclooxygenase-2 inhibitors, compositions and methods of use
INVENTOR(S): Bandarage, Ramani R., Newton, MA, United States
Bandarage, Upul K., Newton, MA, United States
Fang, Xinqin, Lexington, MA, United States
Garvey, David S., Dover, MA, United States
Letts, L. Gordon, Dover, MA, United States
Schroeder, Joseph D., Dedham, MA, United States
Tam, Sang William, Dover, MA, United States

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2001041726	A1	20011115	
	US 6649629	B2	20031118	
APPLICATION INFO.:	US 2000-741816	A1	20001222	(9)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2000-226085P	20000818	(60)
	US 1999-171623P	19991223	(60) <--

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: EDWARD D GRIEFF, HALE & DORR LLP, 1455 PENNSYLVANIA AVE, NW, WASHINGTON, DC, 20004
NUMBER OF CLAIMS: 70
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 5 Drawing Page(s)
LINE COUNT: 6284
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention describes novel nitrosated and/or nitrosylated cyclooxygenase 2 (COX-2) inhibitors and novel compositions comprising at least one nitrosated and/or nitrosylated cyclooxygenase 2 (COX-2) inhibitor, and, optionally, at least one compound that donates, transfers or releases nitric oxide, stimulates endogenous synthesis of nitric oxide, elevates endogenous levels of endothelium-derived relaxing factor or is a substrate for nitric oxide synthase, and/or optionally, at least one therapeutic agent, such as, steroids, nonsteroidal antiinflammatory compounds (NSAID), 5-lipoxygenase (5-LO) inhibitors, leukotriene B.sub.4 (LTB.sub.4) receptor antagonists, leukotriene A.sub.4 (LTA.sub.4) hydrolase inhibitors, 5-HT agonists, 3-hydroxy-3-methylglutaryl coenzyme A (HMGCoA) inhibitors, H antagonists, antineoplastic agents, antiplatelet agents, decongestants, diuretics, sedating or non-sedating anti-histamines, inducible nitric oxide synthase inhibitors, opioids, analgesics, Helicobacter pylori inhibitors, proton pump inhibitors, isoprostane inhibitors, and mixtures thereof. The present invention also provides novel compositions comprising at least one parent COX-2 inhibitor and at least one nitric oxide donor, and, optionally, at least one therapeutic agent. The present invention also provides kits and methods for treating inflammation, pain and fever; for treating and/or improving the gastrointestinal properties of COX-2 inhibitors; for facilitating wound healing; for treating and/or preventing renal toxicity; and for treating and/or preventing other disorders resulting from elevated levels of cyclooxygenase-2.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L40 ANSWER 13 OF 14 USPATFULL on STN

ACCESSION NUMBER: 96:31610 USPATFULL
TITLE: Proteinaceous feed substances having low levels of zinc and high rumen-bypass potentials, and a method for the production thereof
INVENTOR(S): Endres, Joseph G., Fort Wayne, IN, United States
Smith, Janet C., Fort Wayne, IN, United States
Monagle, Charles W., Fort Wayne, IN, United States
PATENT ASSIGNEE(S): Consolidated Nutrition, L.C., Omaha, NE, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5508058		19960416	<--
APPLICATION INFO.:	US 1992-933338		19920821	(7)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Spear, Frank
LEGAL REPRESENTATIVE: Banner & Allegretti, Ltd.
NUMBER OF CLAIMS: 4
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 9 Drawing Figure(s); 9 Drawing Page(s)
LINE COUNT: 718
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Vegetable meal compositions having high-rumen bypass potentials for use in the feeding of ruminant animals, and a method for producing the compositions are claimed. The claimed compositions comprise a protein meal and low levels of zinc ions, with the zinc ions being present in an amount sufficient to provide about 0.003-0.008 parts zinc ions per part of protein in the meal. The composition has a rumen bypass potential, as measured by the "Percent of Total Protein that is Available and Undegraded", or "% AUN", of not less than about 30. The method for producing the composition comprises treating the meals with low levels of zinc ions and heating the mixture under moist heat conditions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L40 ANSWER 14 OF 14 USPATFULL on STN
ACCESSION NUMBER: 95:99079 USPATFULL
TITLE: Multienzyme powdered composition containing bacteria for treatment of waste
INVENTOR(S): Bruno, Mark, Raleigh, NC, United States
PATENT ASSIGNEE(S): Enzyme Research & Development Corporation, Gilberts, IL, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5464766		19951107	<--
APPLICATION INFO.:	US 1994-222108		19940404	(8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Naff, David M.
ASSISTANT EXAMINER: Ware, Deborah K.
LEGAL REPRESENTATIVE: Tolpin, Thomas W.
NUMBER OF CLAIMS: 7
EXEMPLARY CLAIM: 1
LINE COUNT: 980
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A stabilized dust-free powdered enzyme/bacterial fermentation product is provided for readily treating drains, septic tanks, distribution boxes,

holding tanks, drain fields, sewer lines, dry wells, grease traps, compost heaps, and garbage disposals. The stabilized powdered formulation effectively digests and liquifies most organic wastes flushed into on-site waste disposal systems. The environmentally attractive product can also be used for regular periodic sludge pumpouts. The waste-digesting composition can include: enzymes, enzyme preservatives, enzyme activators, nonpathogenic aerobic and anaerobic bacteria, bacterial nutrients, buffers, emulsifiers, and heavy metal scavengers. In a preferred embodiment the composition contains multiple enzymes having less than 26% by weight of the total weight of the composition, and specifically 0.1% to 15% protease, 0.1% to 15% amylase, 0.1% to 15% cellulase, 0.1% to 15% lipase, 0.1% to 15% Bacillus species, 0.1% to 20% phosphate-containing buffer compounds, such as monosodium phosphate, 1% to 20% enzyme preservative, and 0.1% to 10% ion scavenger compounds, as well as 50% to 95% dendritic salts also providing a buffering effect for the composition.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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=> d que stat l47
L19          49 SEA FILE=HCAPLUS ABB=ON  ("MANGEL ALLEN W"/AU OR "MANGEL ALLEN
                WAYNE"/AU)
L20          88 SEA FILE=HCAPLUS ABB=ON  ("NAYLOR ALAN"/AU OR "NAYLOR ALAN
                ROBERT"/AU)
L21           2 SEA FILE=HCAPLUS ABB=ON  L19 AND L20
L22          19 SEA FILE=REGISTRY ABB=ON  (123653-11-2/BI OR 158205-05-1/BI OR
                162011-90-7/BI OR 169590-42-5/BI OR 180200-68-4/BI OR 181695-72
                -7/BI OR 183610-65-3/BI OR 189954-66-3/BI OR 198470-84-7/BI OR
                202409-33-4/BI OR 220991-20-8/BI OR 221148-46-5/BI OR 267235-56
                -3/BI OR 342651-37-0/BI OR 51803-78-2/BI OR 80937-31-1/BI OR
                329900-75-6/BI OR 329967-85-3/BI OR 81098-60-4/BI)
L23           2 SEA FILE=HCAPLUS ABB=ON  L21 AND L22
L24             ANALYZE  L23 1 CT :       15 TERMS
L26          11 SEA FILE=REGISTRY ABB=ON  (CELECOXIB OR ROFECOXIB OR VALDECOXIB
                 OR PARECOXIB OR COX 189 OR ETORICOXIB OR JTE-522 OR JTE522 OR
                DFP OR NS398 OR NS 398 OR L-745337 OR L745337)/CN
L27           1 SEA FILE=REGISTRY ABB=ON  "JTE 522"/CN
L28           1 SEA FILE=REGISTRY ABB=ON  "NS 398"/CN
L29           1 SEA FILE=REGISTRY ABB=ON  "L 745337"/CN
L30           0 SEA FILE=REGISTRY ABB=ON  L24
L31          13 SEA FILE=REGISTRY ABB=ON  L30 OR L26 OR L27 OR L28 OR L29
L32        7710 SEA FILE=HCAPLUS ABB=ON  L31 OR (?CELECOXIB? OR ?ROFECOXIB? OR
                ?VALDECOXIB? OR ?PARECOXIB? OR COX-189 OR COX 189 OR ?ETORICOXI
                B? OR MK663 OR MK 663 OR JTE522 OR JTE 522 OR DFP OR NS398 OR
                NS 398 OR L745337 OR L 745337)
L34          30 SEA FILE=HCAPLUS ABB=ON  L32 AND (?DYSPEPS? OR ?INDIGEST?)
L37           1 SEA FILE=HCAPLUS ABB=ON  L34 AND ?ESOPHAG?(W)?REFLUX?
L38          30 SEA FILE=HCAPLUS ABB=ON  L34 OR L37
L39           5 SEA FILE=HCAPLUS ABB=ON  L38 AND (PRD<20000201 OR PD<20000201)
L41          45 SEA L39
L42          45 DUP REMOV L41 (0 DUPLICATES REMOVED)
L45          44 SEA L42 AND ?HUMAN?
L47          44 SEA L45 AND (?DYSPEPSIA? OR ?INDIGEST?)

=> d ibib abs l47 1-44

L47  ANSWER 1 OF 44  BIOSIS  COPYRIGHT (c) 2005 The Thomson Corporation  on STN
ACCESSION NUMBER:    1999:439273  BIOSIS
DOCUMENT NUMBER:     PREV199900439273
TITLE:               Selective cyclooxygenase-2 inhibitors for the treatment of
                     arthritis.
AUTHOR(S):           Fung, Horatio B.; Kirschenbaum, Harold L. [Reprint author]
CORPORATE SOURCE:    Arnold and Marie Schwartz College of Pharmacy and Health
                     Sciences, Long Island University, 75 DeKalb Avenue,
                     Brooklyn, NY, 11201, USA
SOURCE:              Clinical Therapeutics, (July, 1999) Vol. 21, No.
                     7, pp. 1131-1157. print.
                     CODEN: CLTHDG. ISSN: 0149-2918.
DOCUMENT TYPE:       Article
                     General Review; (Literature Review)
LANGUAGE:            English
ENTRY DATE:          Entered STN: 18 Oct 1999
                     Last Updated on STN: 18 Oct 1999
AB   The purpose of this paper is to review the rationale for a new class of
     nonsteroidal anti-inflammatory drugs (NSAIDs) known as selective
     cyclooxygenase (COX)-2 inhibitors and to present preliminary clinical data
     on 2 COX-2 inhibitors that are approved for use in the United States.  The
     primary mechanism of NSAIDs in the treatment of inflammation is the
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inhibition of COX, which exists in 2 forms. COX-1 appears to regulate many normal physiologic functions, and COX-2 mediates the inflammatory response. Theoretically, an NSAID that inhibits COX-2 selectively should decrease inflammation but not influence normal physiologic functions and thus should cause fewer gastrointestinal side effects. Preliminary data suggest that **celecoxib**, a highly selective COX-2 inhibitor, is superior to placebo and similar to traditional NSAIDs in the short-term treatment of pain due to osteoarthritis, although it has been associated with adverse effects such as headache, change in bowel habits, abdominal discomfort, and dizziness. **Celecoxib** also has been shown to be as effective as traditional NSAIDs in the treatment of rheumatoid arthritis, but it may cause fewer adverse effects, including endoscopically documented ulcers. **Celecoxib** is metabolized in the liver by the cytochrome P-450 isozyme CYP2C9, and thus serious drug interactions are possible. In the treatment of osteoarthritis, **rofecoxib** has been shown to be as effective as traditional NSAIDs and may cause fewer endoscopically documented ulcers, but its complete adverse-effect profile is not known. Until the selective COX-2 inhibitors are widely used and more clinical as well as pharmacoeconomic studies are published, the exact role of COX-2 therapy cannot be determined.

L47 ANSWER 2 OF 44 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2001201645 EMBASE
TITLE: The treatment of peptic ulcer disease.
AUTHOR: Louw J.A.; Marks I.N.
CORPORATE SOURCE: Dr. J.A. Louw, E23 Gastrointestinal Clinic, New Groote Schuur Hospital, Observatory, Cape Town 7925, South Africa. jalouw@curie.uct.ac.za
SOURCE: Current Opinion in Gastroenterology, (**2000**) Vol. 16, No. 6, pp. 489-494.
Refs: 45
ISSN: 0267-1379 CODEN: COGAEK
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 006 Internal Medicine
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20010622
Last Updated on STN: 20010622

AB There is a continuation of the debate on the management of **dyspepsia** while the role of Helicobacter pylori in duodenal ulcer disease is being questioned with renewed vigor, specifically in the United States. The interaction of NSAIDs and H. pylori provided some interesting, if at times confusing, literature while the debate on the safety of long-term acid suppression remained unresolved. There were some interesting developments with regard to therapeutic agents during this period. A fourth proton pump inhibitor was introduced to the market while cisapride, a drug previously considered safe, was effectively withdrawn from the North American market because of safety concerns. More data on the COX-1-sparing agents became available, and their impressive gastrointestinal safety profile was confirmed. It was noted, however, that the incidence of **dyspepsia**, experienced by users of these drugs, may remain a problem. .COPYRGT. 2000 Lippincott Williams & Wilkins, Inc.

L47 ANSWER 3 OF 44 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2001128091 EMBASE
TITLE: **Rofecoxib.** A disappointing nsaid analgesic.
SOURCE: Prescrire International, (**2000**) Vol. 9, No. 50, pp. 166-169.
Refs: 16
ISSN: 1167-7422 CODEN: PRINFU
COUNTRY: France
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Pharmacology
031 Arthritis and Rheumatism
037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20010419
Last Updated on STN: 20010419

AB **Rofecoxib**, a nonsteroidal antiinflammatory drug, is licensed in France for symptom relief in osteoarthritis. It is promoted by MSD-Chibret as a "specific inhibitor of type 2 cyclooxygenases (COX-2)". The clinical dossier includes trials versus other antiinflammatory drugs, but the reports available are generally vague. **Rofecoxib** has not been compared with paracetamol. In these trials **rofecoxib** 12.5-25 mg/day was no more effective than the comparators (ibuprofen or diclofenac) used at maximal recommended doses. Relative to other nonsteroidal antiinflammatory drugs prescribed at high doses to selected patients in the controlled conditions of clinical trials, **rofecoxib** only moderately reduces the risk of severe gastrointestinal reactions (1.3% versus 1.8% after a year of treatment) and dyspeptic disorders (23.5% versus 25.5). Questions persist on other adverse effects, especially those potentially affecting the kidneys and heart. **Rofecoxib** is subject to the same precautions (pregnancy, interactions, etc.) as other nonsteroidal antiinflammatory drugs.

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ACCESSION NUMBER: 2001107053 EMBASE
TITLE: Pharmacological basis for the therapy of pain and inflammation with nonsteroidal anti-inflammatory drugs.
AUTHOR: Steinmeyer J.
CORPORATE SOURCE: Dr. J. Steinmeyer, Department of Orthopaedic Surgery, Justus-Liebig-University of Giessen, Paul-Meimberg-Strasse 3, D-35385 Giessen, Germany. juergen.steinmeyer@ortho.med.uni-giessen.de
SOURCE: Arthritis Research, (**2000**) Vol. 2, No. 5, pp. 379-385.
Refs: 64
ISSN: 1465-9905 CODEN: ARRECG
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 030 Pharmacology
031 Arthritis and Rheumatism
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 20010406
Last Updated on STN: 20010406

AB Nonsteroidal anti-inflammatory drugs (NSAIDs) belong to the most frequently used drugs. The discovery of an inducible isoform of cyclo-oxygenase (COX-2) has led to an intensive worldwide search and the introduction of selective COX-2 inhibitors. In this review, recent advances in understanding the mechanism of action of NSAIDs and, in this context, clinical findings on NSAID-induced gastrointestinal side effects are summarized. This knowledge is important for the effective treatment of pain and inflammation, as well as for preventing serious and sometimes lethal gastrointestinal side effects.

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ACCESSION NUMBER: 2001087355 EMBASE
TITLE: Overview of the arthritis cost consequence evaluation system (ACCES): A pharmacoeconomic model for **celecoxib.**
AUTHOR: Pettitt D.; Goldstein J.L.; McGuire A.; Schwartz J.S.; Burke T.; Maniadakis N.
CORPORATE SOURCE: D. Pettitt, Outcomes Research, Pfizer Inc., New York, NY, United States
SOURCE: Rheumatology, (**2000**) Vol. 39, No. SUPPL. 2, pp. 33-42.
Refs: 53
ISSN: 1462-0324 CODEN: RUMAFK
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 031 Arthritis and Rheumatism
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322

AB Pharmacoeconomic analyses have become useful and essential tools for health care decision makers who increasingly require such analyses prior to placing a drug on a national, regional or hospital formulary. Previous health economic models of non-steroidal anti-inflammatory drugs (NSAIDs) have been restricted to evaluating a narrow range of agents within specific health care delivery systems using medical information derived from homogeneous clinical trial data. This paper summarizes the Arthritis Cost Consequence Evaluation System (ACCES)-a pharmacoeconomic model that has been developed to predict and evaluate the costs and consequences associated with the use of **celecoxib** in patients with arthritis, compared with other NSAIDs and NSAIDs plus gastroprotective agents. The advantage of this model is that it can be customized to reflect local practice patterns, resource utilization and costs, as well as provide context-specific health economic information to a variety of providers and/or decision makers.

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ACCESSION NUMBER: 2001087353 EMBASE
TITLE: **Celecoxib** clinical profile.
AUTHOR: Tive L.
CORPORATE SOURCE: L. Tive, Clinical Research, Pfizer Inc., New York, NY,

United States
SOURCE: Rheumatology, (**2000**) Vol. 39, No. SUPPL. 2, pp. 21-28.
Refs: 53
ISSN: 1462-0324 CODEN: RUMAFK
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Pharmacology
031 Arthritis and Rheumatism
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322

AB **Celecoxib** is the first COX-2-specific inhibitor approved for relief of the signs and symptoms of osteoarthritis (OA) and rheumatoid arthritis (RA), as well as for treatment of familial adenomatous polyposis. For both OA and RA, **celecoxib** has been shown to be significantly superior in efficacy to placebo and similar in efficacy to traditional non-steroidal anti-inflammatory drugs. Its advantage, however, is its gastrointestinal (GI) safety. Randomized clinical trials as well as long-term outcomes studies have demonstrated that the GI safety profile of **celecoxib** is superior to that of traditional NSAIDs and similar to that of placebo. Additionally, the renal and cardiovascular safety of **celecoxib** has also become apparent, as well as its efficacy, tolerability and safety in the elderly population.

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ACCESSION NUMBER: 2001087352 EMBASE
TITLE: Epidemiology and pharmacoeconomic implications of non-steroidal anti-inflammatory drug-associated gastrointestinal toxicity.
AUTHOR: MacDonald T.M.
CORPORATE SOURCE: T.M. MacDonald, Medicines Monitoring Unit, Dept. of Clin. Pharmacol./Therap., Ninewells Hospital/Medical School, Dundee, United Kingdom
SOURCE: Rheumatology, (**2000**) Vol. 39, No. SUPPL. 2, pp. 13-20.
Refs: 61
ISSN: 1462-0324 CODEN: RUMAFK
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 017 Public Health, Social Medicine and Epidemiology
031 Arthritis and Rheumatism
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322

AB Non-steroidal anti-inflammatory drugs (NSAIDs) are widely prescribed and used, especially to treat patients with osteoarthritis and rheumatoid arthritis. Since their introduction as a therapeutic class, a large body of literature has accumulated on the side-effects of these drugs. NSAIDs,

through their inhibition of prostaglandin synthesis, can affect the renal and cardiovascular systems. However, the majority of reported side-effects are related to the gastrointestinal (GI) system, and the occurrence of these GI events adds significantly to the disease burden. Several factors have been identified that contribute to the risk of an NSAID-associated GI event. However, when considering risk, especially in clinical trials or observational studies, it is necessary to distinguish between baseline risk and NSAID-attributable risk, since this distinction can affect the results and conclusions of the study; NSAID-attributable risk is present in subjects who have few or no risk factors for upper GI toxicity. Safer NSAIDs, such as the new specific cyclooxygenase-2 inhibitors, when targeted to the appropriate patient (i.e. those with NSAID-attributable risk), should lead to improved outcomes and reduced costs.

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ACCESSION NUMBER: 2001054457 EMBASE
TITLE: **Celecoxib** - Is it worth celebrating?.
AUTHOR: Taylor B.; van de Wal B.; Mbewu A.
SOURCE: South African Medical Journal, (**2000**) Vol. 90, No. 12, pp. 1188-1192.
Refs: 21
ISSN: 0038-2469 CODEN: SAMJAF
COUNTRY: South Africa
DOCUMENT TYPE: Journal; Note
FILE SEGMENT: 031 Arthritis and Rheumatism
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
ENTRY DATE: Entered STN: 20010223
Last Updated on STN: 20010223
DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L47 ANSWER 9 OF 44 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2001015571 EMBASE
TITLE: [Pharmacological treatment of migraine: A review]. TRATAMENTO FARMACOLOGICO DA MIGRANEA: UMA REVISAO.
AUTHOR: Schmidt A.P.; Schmidt A.P.; Schmidt S.R.G.
SOURCE: Revista Brasileira de Neurologia, (**2000**) Vol. 36, No. 5-6, pp. 127-133.
Refs: 68
ISSN: 0101-8469 CODEN: RBNEE5
COUNTRY: Brazil
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 006 Internal Medicine
008 Neurology and Neurosurgery
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: Portuguese
SUMMARY LANGUAGE: English; Portuguese
ENTRY DATE: Entered STN: 20010125
Last Updated on STN: 20010125

AB Migraine is a disorder characterized by episodic headache associated to symptoms such as nausea, vomiting, photophobia, phonophobia and malaise. Is one the most common complaints encountered by primary-care physicians and neurologists, with a prevalence estimated in 12% and predominance of

women. It is a disturbance that may incapacitate the patients to perform usual activities. There are three main forms of management of this disease: avoid potential trigger factors of the headache, effective treatment of acute attacks with appropriate medications and regular use of preventive medications. Although changes in lifestyle and nonpharmacological alternatives may help to prevent some attacks, the mainstay of treatment is the precocious use of medications. Nowadays there is a wide variety of available drugs, including since the nonsteroidal anti-inflammatory drugs until novel drugs more effective such as the serotoninergic 5HT1B/1D agonists or triptans. The aim of this review is summarize data present in the literature about the various available pharmacological strategies for the acute and preventive treatment of migraine.

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ACCESSION NUMBER: 2001013358 EMBASE
TITLE: [Rational use of **rofecoxib**].
USO RACIONAL DE **ROFECOXIB.**
AUTHOR: Alvaro-Gracia Alvaro J.M.; Gonzalez Enriquez J.; Ramirez Arrizabalaga R.; Sanmarti Sala R.; Villasante Claudios F.; Ferre de la Pena P.
CORPORATE SOURCE: J.M. Alvaro-Gracia Alvaro, Servicio de Reumatologia, Hosp. Universitario de la Princesa, Madrid, Spain
SOURCE: Atencion Primaria, (**2000**) Vol. 26, No. 9, pp. 633-635.
Refs: 9
ISSN: 0212-6567 CODEN: ATEPEY
COUNTRY: Spain
DOCUMENT TYPE: Journal; (Short Survey)
FILE SEGMENT: 031 Arthritis and Rheumatism
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: Spanish
ENTRY DATE: Entered STN: 20010125
Last Updated on STN: 20010125
DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L47 ANSWER 11 OF 44 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2000423898 EMBASE
TITLE: [Two new COX 2 inhibitors: **Celecoxib** and **rofecoxib**].
DOS NOUS INHIBIDORS DE LA COX 2: **CELECOXIB** I **ROFECOXIB.**
AUTHOR: Arenas M.T.
SOURCE: Circular Farmaceutica, (**2000**) Vol. 58, No. 2, pp. 14-18.
Refs: 9
ISSN: 0009-7314 CODEN: CIFAA3
COUNTRY: Spain
DOCUMENT TYPE: Journal; (Short Survey)
FILE SEGMENT: 006 Internal Medicine
030 Pharmacology
031 Arthritis and Rheumatism
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: Catalan
ENTRY DATE: Entered STN: 20001221

Last Updated on STN: 20001221
DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L47 ANSWER 12 OF 44 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2000400546 EMBASE
TITLE: Evaluation of intravenous **parecoxib** for the relief of acute post-surgical pain.
AUTHOR: Jain K.K.
CORPORATE SOURCE: K.K. Jain, Jain PharmaBiotech, Blasiring 7, CH-1057 Basel, Switzerland. jain@pharmabiotech.ch
SOURCE: Expert Opinion on Investigational Drugs, (**2000**) Vol. 9, No. 11, pp. 2717-2723.
Refs: 19
ISSN: 1354-3784 CODEN: EOIDER
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 009 Surgery
024 Anesthesiology
030 Pharmacology
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20001213
Last Updated on STN: 20001213

AB **Parecoxib** is a prodrug of **valdecoxib**, which is a potent and selective inhibitor of COX-2. Intravenous preparation of **parecoxib** is in Phase III clinical trials for the management of acute and severe post-surgical pain. It is the only COX-2 inhibitor that is available in a parenteral formulation. Clinical results compare **parecoxib** with ketorolac, a NSAID, which is the only non-narcotic analgesic available in parenteral formulation that can be administered for the relief of moderate to severe acute pain. Pharmacokinetic studies have shown that **parecoxib** is converted to **valdecoxib** within a short time following administration by im. or iv. injection. In clinical trials, **parecoxib** compares favourably with ketorolac and produces less gastric or duodenal ulcers, the predominant adverse effect, than ketorolac. **Parecoxib**, thus, fulfils some of the desirable characteristics of an ideal non-narcotic analgesic for severe post-surgical pain and has application in other acutely painful conditions. **Parecoxib** is expected to be file for approval before the end of 2000 and is expected to be introduced in the market in 2001. It has favourable prospects for a fair share of the post-surgical pain relief market which is valued at approximately US$ 1 billion for the year 2000.

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ACCESSION NUMBER: 2000361824 EMBASE
TITLE: Significant upper gastrointestinal events associated with conventional NSAID versus **celecoxib.**
AUTHOR: Goldstein J.L.
CORPORATE SOURCE: Dr. J.L. Goldstein, Section of Digestive/Liver Diseases, Department of Medicine, 840 South Wood Street, Chicago, IL 60612-7323, United States
SOURCE: Journal of Rheumatology, (**2000**) Vol. 27, No. SUPPL. 60, pp. 25-28.

Refs: 25
ISSN: 0315-162X CODEN: JRHUA
COUNTRY: Canada
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 031 Arthritis and Rheumatism
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20001102
Last Updated on STN: 20001102

AB Despite their substantial clinical benefits in the management of rheumatoid arthritis, osteoarthritis, pain, and other musculoskeletal complaints, conventional nonsteroidal antiinflammatory drugs (NSAID) are associated with significant toxicities that can frequently limit their use. The most common and noteworthy adverse effects of NSAID are gastrointestinal (GI), and range from dyspeptic symptoms to ulcers and serious ulcer complications. The upper GI toxicities associated with the use of conventional NSAID led to the search for medications that were as clinically effective as these agents, but with a significantly improved GI safety profile. It is now known that the constitutively expressed isoenzyme cyclooxygenase (COX)-1 catalyzes the synthesis of prostanoids that help to regulate normal physiologic processes, including GI mucosa protection, whereas the inducible isoenzyme COX-2 leads to the generation of prostaglandins that mediate inflammation, pain, and fever. This knowledge has led to the development of new compounds that, at therapeutic concentrations, inhibit COX-2 without affecting COX-1. The first COX-2 targeted agent approved by the US Food and Drug Administration (FDA) was **celecoxib.** This article reviews the risks of GI complications associated with conventional NSAID use and compares these risks with that of the new COX-2 specific inhibitor **celecoxib.**

L47 ANSWER 14 OF 44 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2000336900 EMBASE
TITLE: Nonsteroidal anti-inflammatory drugs.
AUTHOR: Tseng C.-C.; Wolfe M.M.
CORPORATE SOURCE: Dr. M.M. Wolfe, Boston Medical Center, Section of Gastroenterology, EBRC 507, 650 Albany Street, Boston, MA 02118-2393, United States. michael.wolfe@bmc.org
SOURCE: Medical Clinics of North America, **(2000)** Vol. 84, No. 5, pp. 1329-1344.
Refs: 72
ISSN: 0025-7125 CODEN: MCNAA
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20001005
Last Updated on STN: 20001005

AB NSAID-associated dyspeptic symptoms are common and can be managed empirically with an H2-receptor antagonist or a proton-pump inhibitor. Treatment of established gastroduodenal ulcers is accomplished best by withholding the offending drugs. Proton-pump inhibitors appear to heal ulcers at the same rate whether or not NSAID therapy is continued. After the ulcer is healed and if NSAID therapy must be continued, prophylaxis is

accomplished best by the concomitant use of proton-pump inhibitors, misoprostol (at least 200 μg 3 times a day), or a NSAID that preferentially inhibits COX-2. The future development of newer, safer NSAID preparations, including highly selective COX-2 inhibitors and nitric oxide-releasing NSAIDs, should provide better treatment options for the increasing number of individuals requiring anti-inflammatory agents.

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ACCESSION NUMBER: 2000335442 EMBASE
TITLE: Selective Cox-2 inhibition in man - Therapeutic breakthroughor cosmetic advance?.
AUTHOR: Wollheim F.A.
CORPORATE SOURCE: F.A. Wollheim, Lund University Hospital, SE-221 85 Lund, Sweden
SOURCE: Rheumatology, (**2000**) Vol. 39, No. 9, pp. 935-938.
Refs: 47
ISSN: 1462-0324 CODEN: RUMAFK
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Editorial
FILE SEGMENT: 030 Pharmacology
031 Arthritis and Rheumatism
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
ENTRY DATE: Entered STN: 20001013
Last Updated on STN: 20001013
DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L47 ANSWER 16 OF 44 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2000312731 EMBASE
TITLE: Upper gastrointestinal tolerability of **celecoxib**, a COX-2 specific inhibitor, compared to naproxen and placebo.
AUTHOR: Bensen W.G.; Zhao S.Z.; Burke T.A.; Zabinski R.A.; Makuch R.W.; Maurath C.J.; Agrawal N.M.; Geis G.S.; Bucciarelli K.
CORPORATE SOURCE: Dr. W.G. Bensen, Pharmacia, 5200 Old Orchard Road (00-2-2), Skokie, IL 60077, United States
SOURCE: Journal of Rheumatology, (**2000**) Vol. 27, No. 8, pp. 1876-1883.
Refs: 49
ISSN: 0315-162X CODEN: JRHUA
COUNTRY: Canada
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 031 Arthritis and Rheumatism
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20000921
Last Updated on STN: 20000921

AB Objective. To determine the upper gastrointestinal (GI) tolerability of **celecoxib**, naproxen, and placebo in patients with rheumatoid arthritis (RA) and osteoarthritis (OA). Methods. An analysis of 5, 12-week, randomized, double blind, parallel group, placebo controlled clinical trials was conducted. In these trials, patients were randomized to: naproxen 500 mg bid (n = 1099), placebo (n = 1136), **celecoxib** 50 mg bid (n = 690) (subtherapeutic dose), **celecoxib** 100 mg (n =

1131) or 200 mg bid (n = 1125) (therapeutic dose), or **celecoxib** 400 mg bid (n = 434) (supratherapeutic dosage). The incidence and time until moderate to severe abdominal pain, **dyspepsia**, nausea, and any of the aforementioned 3 upper GI symptoms (composite endpoint) were determined using time-to-event analysis. Results. The cumulative incidences of moderate to severe abdominal pain, **dyspepsia**, or nausea (composite endpoint) were: naproxen 500 mg (12.0%; 95% CI 9.9%-14.0%), **celecoxib** 50 mg bid (7.1%; 95% CI 5.0%-9.2%), **celecoxib** 100 mg bid (7.8%; 95% CI 6.0%-9.5%), **celecoxib** 200 mg bid (8.1%; 95% CI 6.4%-9.9%), **celecoxib** 400 mg bid (6.0%; 95% CI 3.6%-8.4%), and placebo (8.5%; 95% CI 6.5%-10.8%). After controlling for independent predictors of the composite endpoint, relative risks (RR) for the various treatments relative to naproxen 500 mg bid were: **celecoxib** 50 mg (RR 0.54; 95% CI 0.37-0.77; p < 0.001), **celecoxib** 100 mg (RR 0.60; 95% CI 0.45-0.80; p < 0.001), **celecoxib** 200 mg bid (RR 0.63; 95% CI 0.47-0.83; p = 0.001), **celecoxib** 400 mg bid (RR 0.56; 95% CI 0.35-0.89; p = 0.015), and placebo (RR 0.63; 95% CI 0.47-0.85; p = 0.002). After controlling for independent predictors of the composite endpoint, **celecoxib** treatment group patients did not differ from placebo patients when reporting the composite endpoint, with p values ranging from 0.40 to 0.96. Conclusion. The upper GI tolerability of **celecoxib** is superior to naproxen. A dose-response relationship between **celecoxib** and upper GI symptoms was not apparent.

L47 ANSWER 17 OF 44 EMBASE
on STN

ACCESSION NUMBER: 2000283530 EMBASE
TITLE: Nonsteroidal anti-inflammatory drug gastropathy.
AUTHOR: Hawkey C.J.
CORPORATE SOURCE: Dr. C.J. Hawkey, Division of Gastroenterology, University Hospital Nottingham, Queen's Medical Centre, Nottingham, United Kingdom. cj.hawkey@nottingham.ac.uk
SOURCE: Gastroenterology, (**2000**) Vol. 119, No. 2, pp. 521-535.
Refs: 143
ISSN: 0016-5085 CODEN: GASTAB
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20000831
Last Updated on STN: 20000831

AB By inhibiting prostaglandin synthesis, nonsteroidal anti-inflammatory drugs (NSAIDs) compromise gastroduodenal defense mechanism including blood flow and mucus/bicarbonate secretion. This has led to NSAIDs being the most widely reported drug cause of adverse events. While NSAIDs also cause **dyspepsia**, inhibition of prostaglandin synthesis may reduce this from even higher levels that would otherwise prevail and mask ulcer-related **dyspepsia**, making anticipatory management difficult. On average, the risk of ulcer complications increases 4-fold, resulting in 1.25 additional hospitalizations per 100 patient-years according to one estimate. Older patients, those with a past history, and those taking anticoagulants or corticosteroids are at higher risk. Risk is dose dependent and is lower with ibuprofen at low doses than with other NSAIDs. It is unlikely that Helicobacter pylori increases the risk, and

under some circumstances it may be protective. Selective inhibitors of the inducible cyclooxygenase 2 spare gastric mucosal prostaglandin synthesis and do not damage the gastric mucosa. Their place in therapy, compared with use of misoprostol or proton pump inhibitors, is currently emerging. Future competitors may include nitric oxide-donating, zwitterionic, or R-enantiomer NSAIDs.

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ACCESSION NUMBER: 2000263541 EMBASE
TITLE: Pharmacologic considerations for opiate analgesic and nonsteroidal anti-inflammatory drugs.
AUTHOR: Papich M.G.
CORPORATE SOURCE: M.G. Papich, College of Veterinary Medicine, North Carolina State University, 4700 Hillsborough Street, Raleigh, NC 27606, United States
SOURCE: Veterinary Clinics of North America - Small Animal Practice, (2000) Vol. 30, No. 4, pp. 815-837.
Refs: 132
ISSN: 0195-5616 CODEN: VCNAA6
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20000817
Last Updated on STN: 20000817

AB When administering opioid analgesic drugs or nonsteroidal anti-inflammatory drugs, veterinarians are often not familiar enough with the underlying pharmacology of the drugs, particularly with the potential for drug interactions and adverse effects. This article considers some of the pharmacologic features of these drugs and provides a basis for important interactions, contraindications, and adverse effects.

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ACCESSION NUMBER: 2000228354 EMBASE
TITLE: Inhibitors of cyclooxygenase-2: November 1999-April 2000.
AUTHOR: Carter J.S.
CORPORATE SOURCE: J.S. Carter, Pharmacia Corp., 700 Chesterfield Parkway North, St. Louis, MO 63198, United States
SOURCE: Expert Opinion on Therapeutic Patents, (2000) Vol. 10, No. 7, pp. 1011-1020.
Refs: 56
ISSN: 1354-3776 CODEN: EOTPEG
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20000720
Last Updated on STN: 20000720

AB Since the discovery of aspirin, the search for safer and more efficacious agents for the treatment of inflammation, pain and fever has continued for more than a century. Agents such as aspirin, the first synthetic NSAID,

exert their effect by inhibiting the conversion of arachidonic acid to prostaglandins via the cyclooxygenase (COX) enzyme pathway. Beyond their therapeutic utility, traditional NSAIDs possess predictable side effects including **dyspepsia**, GI ulceration and antiplatelet activity.
It is now well established that two isoforms of COX exist. COX-1 is constitutively formed and is responsible for production of basal levels of prostaglandins needed for GI tract homeostasis, proper renal filtration rate and platelet aggregatory function. Biosynthesis of the COX-2 enzyme is induced by pro-inflammatory stimuli such as IL-1, TNF-α, growth factors and endotoxin LPS. The elevated levels of prostaglandins produced by the newly formed COX-2 cause the pathologic symptoms of inflammation. Favourably, specific COX-2 inhibitors display efficacy as analgesic and anti-inflammatory agents without causing GI damage and antiplatelet activity demonstrated by traditional, non-selective NSAIDs. The decreased GI side effect profile may explain the rapid acceptance of the first two COX-2 inhibitors marketed, **celecoxib** and **rofecoxib**, which garnered over US$2 billion from their combined partial year of sales in 1999. COX-2 specific agents, due to their higher therapeutic index, can be studied at levels in excess of their therapeutic, anti-inflammatory dosage. Consequently, many new areas of research have become available. Pivotal preclinical and clinical research in the chemoprevention and treatment of cancer and the treatment of Alzheimer's disease is in progress. This review will cover the recent patent literature (November 1999-April 2000) including new chemical classes and new filings on previously disclosed series.

L47 ANSWER 20 OF 44 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2000208518 EMBASE
TITLE: Basic biology and clinical application of specific cyclooxygenase-2 inhibitors.
AUTHOR: Crofford L.J.; Lipsky P.E.; Brooks P.; Abramson S.B.; Simon L.S.; Van de Putte L.B.A.
CORPORATE SOURCE: Dr. L.J. Crofford, University of Michigan, 5510E MSRB I, 1150 West Medical Center Drive, Ann Arbor, MI 48109-0680, United States
SOURCE: Arthritis and Rheumatism, (**2000**) Vol. 43, No. 1, pp. 4-13.
Refs: 85
ISSN: 0004-3591 CODEN: ARHEAW
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 031 Arthritis and Rheumatism
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20000706
Last Updated on STN: 20000706

AB In summary, COX-2 is a highly regulated gene product that catalyzes the local production of PGs in pathologic and physiologic situations (Figure 1). It is clear that COX-2 is the isoform responsible for production of the PGs that mediate inflammation, pain, and fever. However, the role for COX-2 in normal physiology is still being defined. Specific COX-2 inhibitors represent a significant conceptual advance in therapy for patients with arthritis. Although there is no expectation of superior efficacy, clinical trials suggest that efficacy will be comparable with that of nonselective NSAIDs. Clinical trials demonstrate the potential for clinically meaningful reductions in the incidence of the most serious

GI complications found with nonselective NSAIDs, i.e., ulcer, perforation, and GI bleeding. Over the next several years, treatment of large numbers of patients with specific COX-2 inhibitors will help to define the biology of COX-2. The magnitude of this advance in the therapy of rheumatic diseases is yet to be accurately determined, but the development of specific COX-2 inhibitors may afford significant new treatment options for many patients.

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ACCESSION NUMBER: 2000160264 EMBASE
TITLE: Treatment of osteoarthritis with **celecoxib**, a cyclooxygenase-2 inhibitor: A randomized controlled trial.
AUTHOR: Bensen W.G.; Fiechtner J.J.; McMillen J.I.; Zhao W.W.; Yu S.S.; Woods E.M.; Hubbard R.C.; Isakson P.C.; Verburg K.M.; Geis G.S.
CORPORATE SOURCE: Dr. W.G. Bensen, 26 Charlton Ave E, Hamilton, Ont. L8N 1Y2, Canada
SOURCE: Mayo Clinic Proceedings, (**1999**) Vol. 74, No. 11, pp. 1095-1105.
Refs: 45
ISSN: 0025-6196 CODEN: MACPAJ
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 006 Internal Medicine
030 Pharmacology
031 Arthritis and Rheumatism
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20000525
Last Updated on STN: 20000525

AB Objective: To compare the efficacy and safety of **celecoxib**, a cyclooxygenase-2 (COX-2) inhibitor, with those of naproxen, a nonsteroidal anti-inflammatory drug (NSAID), and placebo in the treatment of osteoarthritis of the knee. Methods: In this multicenter, randomized, double- blind, placebo-controlled trial, 1003 patients with symptomatic osteoarthritis of the knee were randomly assigned to receive **celecoxib** at doses of 50, 100, or 200 mg twice a day; naproxen, 500 mg twice a day; or placebo for 12 weeks. Patients were evaluated with standard measures of efficacy 2 to 7 days after discontinuing previous NSAID or analgesic therapy and after 2, 6, and 12 weeks of treatment with the study drug. Results: **Celecoxib** treatment led to significant improvement in the signs and symptoms of osteoarthritis as determined by all efficacy measures. Significant pain relief occurred within 2 days of the initiation of treatment, and maximum anti-inflammatory and analgesic activity, evident within 2 weeks, was sustained throughout the 12-week study. All **celecoxib** doses were efficacious compared with placebo, although the 50-mg twice-daily dosage regimen was minimally effective. The higher doses of **celecoxib** (100 and 200 mg twice a day) were similarly efficacious, and the magnitude of improvement observed with these dosing regimens was comparable to that seen with naproxen at a dose of 500 mg twice a day. All doses of **celecoxib** and naproxen were well tolerated. Conclusion: COX-2 inhibition with **celecoxib** is an effective approach for the treatment of osteoarthritis, as seen by clinical improvement in signs and symptoms comparable to treatment with naproxen.

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ACCESSION NUMBER: 2000149819 EMBASE
TITLE: Meloxicam: A COX-2-specific NSAID for the treatment of osteoarthritis.
AUTHOR: Siepler J.K.
CORPORATE SOURCE: J.K. Siepler, Dept. of Pharmaceutical Services, University of California, Davis Medical Center, San Francisco, CA, United States
SOURCE: Formulary, (**2000**) Vol. 35, No. 4, pp. 317-327.
Refs: 26
ISSN: 1082-801X CODEN: FORMF
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 031 Arthritis and Rheumatism
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20000511
Last Updated on STN: 20000511

AB Meloxicam is a COX-2-specific nonsteroidal anti-inflammatory drug (NSAID) under FDA review for the treatment of osteoarthritis. In vitro studies demonstrate that it has greater COX-2 selectivity than traditional NSAIDs, such as naproxen, but less than the COX-2-specific agents **celecoxib** or **rofecoxib.** In comparative trials in patients with osteoarthritis and rheumatoid arthritis, meloxicam has generally demonstrated similar efficacy to naproxen, diclofenac, and piroxicam. Gastrointestinal adverse reactions appear to be less frequent with meloxicam than with traditional non-COX-2- specific NSAIDs. In two large trials, patients receiving meloxicam experienced significantly less **dyspepsia**, nausea, vomiting, and abdominal pain than those receiving piroxicam or diclofenac. Studies have not yet demonstrated whether the incidence of perforations, ulcerations, and gastrointestinal bleeding is lower with meloxicam than with other NSAIDs. Studies comparing meloxicam with **celecoxib** or **rofecoxib** have not yet been conducted.

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ACCESSION NUMBER: 2000028976 EMBASE
TITLE: Towards a GI safer antiinflammatory therapy.
AUTHOR: Scarpignato C.; Bjarnason I.; Bretagne J.-F.; De Pouvourville G.; Garcia Rodriguez L.A.; Goldstein J.L.; Simon M.B.
CORPORATE SOURCE: Dr. C. Scarpignato, Laboratory of Clinical Pharmacology, Department of Internal Medicine, Maggiore University Hospital, 43100 Parma, Italy. scarpi@tin.it
SOURCE: Gastroenterology International, (**1999**) Vol. 12, No. 4, pp. 186-215.
Refs: 329
ISSN: 0950-5911 CODEN: GASIEG
COUNTRY: Italy
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 030 Pharmacology
031 Arthritis and Rheumatism
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology

052 Toxicology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20000202
Last Updated on STN: 20000202

AB Non-steroidal anti-inflammatory drugs (NSAIDs) are widely prescribed medicines. Although these compounds represent a very effective class of drugs, their use is associated with a broad spectrum of untoward reactions in the liver, kidney, skin and gut. GI problems constitute a wide range of different clinical pictures, ranging from symptoms such as **dyspepsia**, heartburn and abdominal discomfort to more serious events, like peptic ulcer and its life-threatening complications, bleeding and perforation. NSAIDs appear to cause gastroduodenal damage, by two main mechanisms: a physiochemical disruption of the gastric mucosal barrier and a systemic inhibition of gastric mucosal protection, through inhibition of cyclooxygenase (COX) activity of gastrointestinal (GI) mucosa. A reduced synthesis and secretion of mucus and bicarbonate, an impairment of mucosal blood flow and an increase of acid secretion represent the main consequences of NSAID-induced prostaglandin (PG) deficiency. Since PGs are well established modulators of inflammatory response, it is evident that NSAIDs induce damage to GI tract via a mechanism identical to that by which they exert their anti-inflammatory action. In this context, it has been difficult until very recently to imagine an effective NSAID completely devoid of GI side effects and co-therapy with misoprostol and proton pump inhibitors has been used in patients at risk to prevent NSAID-associated ulcers and complications. Although in the past some drugs have been claimed to spare the GI tract, their promises have been mostly unfulfilled. The discovery of two cyclooxygenase isoforms has allowed the development of highly selective COX-2 inhibitors that would spare GI mucosa while retaining antiinflammatory activity. Together with this new class of drugs, now called coxib, several other approaches to the rational design of GI-sparing NSAIDs have shown promise in experimental studies.

L47 ANSWER 24 OF 44 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2000028973 EMBASE
TITLE: Selective inhibitors of COX-2. New therapeutic agents.
AUTHOR: Isakson P.C.; Verburg K.M.; Maziasz T.J.; Geis G.S.
CORPORATE SOURCE: Dr. P.C. Isakson, G.D. Searle and Co., Research and Development, Skokie, IL 60077, United States
SOURCE: Gastroenterology International, (**1999**) Vol. 12, No. 4, pp. 169-177.
Refs: 109
ISSN: 0950-5911 CODEN: GASIEG
COUNTRY: Italy
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 026 Immunology, Serology and Transplantation
030 Pharmacology
031 Arthritis and Rheumatism
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
052 Toxicology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20000202
Last Updated on STN: 20000202

AB Nonsteroidal anti-inflammatory drugs are the cornerstone in the treatment

of inflammatory diseases such as arthritis. Unfortunately, these drugs can cause severe and even life-threatening adverse effects that often limit their therapeutic benefit. Progress toward safer anti-inflammatory therapy was aided by an important breakthrough in the pathophysiology of inflammation: the discovery that cyclooxygenase exists as two isozymes, COX-1 and COX-2. Both isozymes form prostaglandins that support physiological functions; however, the formation of pro-inflammatory prostaglandins is catalyzed by COX-2. Inhibition of COX-2 accounts for the anti-inflammatory and analgesic action of nonsteroidal anti-inflammatory drugs; simultaneous inhibition of COX-1 inhibits prostaglandin-dependent mechanisms such as gastroduodenal mucosal defense and platelet aggregation. This inhibition is the basis of the gastrointestinal toxicity and bleeding characteristic of these drugs. These findings led to the hypothesis that agents that selectively inhibit COX-2 will possess anti-inflammatory and analgesic action, but spare COX-1, thereby avoiding or minimizing adverse effects in the gastrointestinal tract and platelets. Selective COX-2 inhibitors, such as **celecoxib** and **rofecoxib**, are now available in many parts of the world. The novelty of these agents has raised questions in the medical and scientific communities as to what constitutes selectivity for COX-2. This article discusses the criteria that must be met to support characterization of an antiinflammatory agent as COX-2-selective. Importantly, clinical evidence of clear improvement in gastrointestinal tolerability and safety must be demonstrated in addition to complementary evidence of COX-2 selectivity obtained from enzyme, biochemical and clinical pharmacology evaluations.

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ACCESSION NUMBER: 2000005664 EMBASE

TITLE: **Celecoxib** versus diclofenac in long-term management of rheumatoid arthritis: Randomised double-blind comparison.

AUTHOR: Emery P.; Zeidler H.; Kvien T.K.; Guslandi M.; Naudin R.; Stead H.; Verburg K.M.; Isakson P.C.; Hubbard R.C.; Geis G.S.

CORPORATE SOURCE: Dr. G.S. Geis, Searle Research and Development, Skokie, IL 60077, United States. george.s.geis@monsanto.com

SOURCE: Lancet, (**18 Dec 1999**) Vol. 354, No. 9196, pp. 2106-2111.
Refs: 32
ISSN: 0140-6736 CODEN: LANCAO

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 031 Arthritis and Rheumatism
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 20000113
Last Updated on STN: 20000113

AB Background. Non-steroidal anti-inflammatory drugs (NSAIDs) inhibit cyclo-oxygenase (COX), which leads to suppression of COX-1-mediated production of gastrointestinal-protective prostaglandins. Gastrointestinal injury is a common outcome. We compared the efficacy, safety, and tolerability of long-term therapy with **celecoxib**, a COX-1 sparing inhibitor of COX-2, with diclofenac, a non-specific COX inhibitor. Methods. 655 patients with adult-onset rheumatoid arthritis of

at least 6 months' duration were randomly assigned oral **celecoxib** 200 mg twice daily or diclofenac SR 75 mg twice daily for 24 weeks. Anti-inflammatory and analgesic activity and tolerability were assessed at baseline, every 4 weeks, and at week 24. We assessed gastrointestinal safety by upper-gastrointestinal endoscopy within 7 days of the last treatment dose at centres where the procedure was available. Analysis was by intention-to-treat. Findings. 430 patients underwent endoscopy (**celecoxib** n = 212, diclofenac n = 218). The two drugs were similar in management of rheumatoid arthritis pain and inflammation. Gastroduodenal ulcers were detected endoscopically in 33 (15%) patients treated with diclofenac and in eight (4%) in the **celecoxib** group ($p < 0.001$). The rate of withdrawal for any gastrointestinal-related adverse event, most commonly abdominal pain, diarrhoea, and **dyspepsia**, was nearly three times higher in the diclofenac-treated group than in the **celecoxib** group (16 vs 6%; $p < 0.001$). Interpretation. **Celecoxib** showed sustained anti-inflammatory and analgesic activity similar to diclofenac, with a lower frequency of upper gastrointestinal ulceration or gastrointestinal adverse events, and tolerability was better.

L47 ANSWER 26 OF 44 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2000004892 EMBASE
TITLE: Management of NSAID-related gastrointestinal mucosal injury.
AUTHOR: Barrison A.F.; Wolfe M.M.
CORPORATE SOURCE: M.M. Wolfe, Section of Gastroenterology, Boston University School of Medicine, Boston Medical Center, 88 East Newton Street, Boston, MA 02118-2393, United States. michael.wolfe@bmc.org
SOURCE: Inflammopharmacology, (**1999**) Vol. 7, No. 3, pp. 277-286.
Refs: 23
ISSN: 0925-4692 CODEN: IAOAES
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20000113
Last Updated on STN: 20000113

AB The three therapeutic goals in patients with NSAID-induced gastroduodenopathy are treatment of dyspeptic symptoms, management of NSAID- related ulcers and their complications, and prophylaxis against recurrent gastrointestinal toxicity. Both H2-receptor antagonists and proton pump inhibitors (PPIs) appear to be helpful in relieving the symptoms associated with NSAID use, while treatment of NSAID-induced gastroduodenal ulcers, whether the NSAID is continued or not, is best achieved by the use of PPIs. However, because symptoms do not often predict the presence of gastroduodenal ulcers, the goal of prevention has become paramount in the treatment of patients with an increased likelihood of gastrointestinal toxicity. The best prophylaxis against NSAID-related toxicity is the use of an alternative agent such as salsalate or paracetamol (acetaminophen). However, if an NSAID is to be used, prophylaxis is best accomplished with a PPI or misoprostol, a prostaglandin El analogue. The use of misoprostol is limited by its frequent dosing, at least 200 μg three times a day, and its own

gastrointestinal side effects. Future therapy will include NSAIDs that maintain their anti- inflammatory effects, while possessing superior safety profiles, and include preferential and highly selective COX-2 inhibitors and nitric oxide releasing compounds.

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ACCESSION NUMBER: 1999406888 EMBASE
TITLE: COX-1-sparing NSAIDs - Is the enthusiasm justified?.
AUTHOR: Peterson W.L.; Cryer B.
CORPORATE SOURCE: Dr. W.L. Peterson, Veterans Affairs Medical Center, 4500 S Lancaster Rd, Dallas, TX 75216, United States. w.peterson@juno.com
SOURCE: Journal of the American Medical Association, (**24 Nov 1999**) Vol. 282, No. 20, pp. 1961-1963.
Refs: 7
ISSN: 0098-7484 CODEN: JAMAAP
COUNTRY: United States
DOCUMENT TYPE: Journal; Editorial
FILE SEGMENT: 036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
LANGUAGE: English
ENTRY DATE: Entered STN: 19991210
Last Updated on STN: 19991210
DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L47 ANSWER 28 OF 44 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 1999406881 EMBASE
TITLE: Anti-inflammatory and upper gastrointestinal effects of **celecoxib** in rheumatoid arthritis: A randomized controlled trial.
AUTHOR: Simon L.S.; Weaver A.L.; Graham D.Y.; Kivitz A.J.; Lipsky P.E.; Hubbard R.C.; Isakson P.C.; Verburg K.M.; Yu S.S.; Zhao W.W.; Geis G.S.
CORPORATE SOURCE: Dr. L.S. Simon, Beth Israel Deaconess Medical Center, 110 Francis St, Boston, MA 02215, United States
SOURCE: Journal of the American Medical Association, (**24 Nov 1999**) Vol. 282, No. 20, pp. 1921-1928.
Refs: 53
ISSN: 0098-7484 CODEN: JAMAAP
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 031 Arthritis and Rheumatism
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19991210
Last Updated on STN: 19991210

AB Context: In vitro studies have shown that **celecoxib** inhibits cyclooxygenase 2 (COX-2) but not COX-1, suggesting that this drug may have anti-inflammatory and analgesic activity without adverse upper gastrointestinal (GI) tract effects that result from COX-1 inhibition. Objective: To test whether **celecoxib** has efficacy as an anti-inflammatory and analgesic with reduced GI tract mucosal damage compared with conventional nonsteroidal anti-inflammatory drugs in

patients with rheumatoid arthritis. Design: Randomized, multicenter, placebo-controlled, double-blind trial lasting 12 weeks, with follow-up at weeks 2, 6, and 12, from September 1996 thorough February 1998. Setting: Seventy-nine clinical sites in the United States and Canada. Patients: A total of 1149 patients aged 18 years or older with symptomatic rheumatoid arthritis who met inclusion criteria were randomized; 688 (60%) of these completed the study. Interventions: Patients were randomized to receive **celecoxib**, 100 mg, 200 mg, or 400 mg twice per day (n = 240, 235, and 218, respectively); naproxen, 500 mg twice per day (n = 225); or placebo (n = 231). Main Outcome Measures: Improvement in signs and symptoms of rheumatoid arthritis as assessed using standard measures of efficacy and GI tract safety as assessed by upper GI tract endoscopy before and after treatment, compared among treatment groups. Results: All dosages of **celecoxib** and naproxen significantly improved the signs and symptoms of arthritis compared with placebo. Maximal anti-inflammatory and analgesic activity was evident within 2 weeks of initiating treatment and was sustained throughout the 12 weeks. The incidence of endoscopically determined gastroduodenal ulcers in placebo-treated patients was 4 (4%) of 99, and the incidences across all dosages of **celecoxib** were not significantly different (P>.40): 9 (6%) of 148 with 100 mg twice per day, 6 (4%) of 145 with 200 mg twice per day, and 8 (6%) of 130 with 400 mg twice per day. In contrast, the incidence with naproxen was 36 (26%) of 137, significantly greater than either placebo or **celecoxib** (P<.001). The overall incidences of GI tract adverse effects were 19% for placebo; 28%, 25%, and 26% for **celecoxib** 100 mg, 200 mg, and 400 mg twice per day, respectively; and 31% for naproxen. Conclusion: In this study, all dosages of **celecoxib** were efficacious in the treatment of rheumatoid arthritis and did not affect COX-1 activity in the GI tract mucosa as evidenced by less frequent incidence of endoscopic ulcers compared with naproxen.

L47 ANSWER 29 OF 44 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 1999389858 EMBASE
TITLE: Cyclooxygenase-2: A new therapeutic target.
AUTHOR: Sengupta S.
CORPORATE SOURCE: S. Sengupta, Department of Pharmacology, University of Cambridge, Cambridge, United Kingdom
SOURCE: Indian Journal of Pharmacology, (**1999**) Vol. 31, No. 5, pp. 322-332.
Refs: 96
ISSN: 0253-7613 CODEN: INJPD2
COUNTRY: India
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 037 Drug Literature Index
030 Pharmacology
016 Cancer
005 General Pathology and Pathological Anatomy
008 Neurology and Neurosurgery
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19991202
Last Updated on STN: 19991202

AB Cyclooxygenase (COX) is the enzyme catalysing oxidation of arachidonic acid to hydroperoxy endoperoxide (PGG2) and its subsequent reduction to hydroxy endoperoxide (PGH2). It is thus an important therapeutic target for the modulation of the prostaglandin pathway. Recent studies have

demonstrated the existence of a second isoform of COX. Both the isoforms have a molecular weight of 71K with 63% amino acid homology. The **human** COX-2 gene is however a 8.3Kb small immediate early gene and is induced by most of the stimuli associated with inflammation. COX-2 has thus been implicated in pathological roles of COX while constitutive COX-1 is said to be involved in physiological functions. Indeed, COX-2 has now been associated with inflammation, hyperalgesia, angiogenesis, neuromodulation, cancer and Alzheimer's disease, giving rise to the opportunity of modulating these conditions with selective inhibitors of COX-2. The recent X-ray structural analysis for COX-2 has paved the way for development of a whole new range of agents with selectivity for this isoform, thereby sparing the physiological functions. Here in this review, an attempt has been made to elucidate the role of COX-2 in these conditions and to evaluate the various COX-2 inhibitors that are in different stages of development or are presently available. From the present knowledge of COX-1 and COX-2 an effort has been made to reclassify NSAIDs based on the selectivity in inhibiting the isoforms.

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ACCESSION NUMBER: 1999389476 EMBASE
TITLE: The safety profile, tolerability, and effective dose range of **rofecoxib** in the treatment of rheumatoid arthritis.
AUTHOR: Schnitzer T.J.; Truitt K.; Fleischmann R.; Dalgin P.; Block J.; Zeng Q.; Bolognese J.; Seidenberg B.; Ehrich E.W.
CORPORATE SOURCE: Dr. K. Truitt, Merck Research Laboratories, RY 32-645, 126 East Lincoln Avenue, Rahway, NJ 07065, United States
SOURCE: Clinical Therapeutics, (**1999**) Vol. 21, No. 10, pp. 1688-1702.
Refs: 51
ISSN: 0149-2918 CODEN: CLTHDG
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 031 Arthritis and Rheumatism
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19991202
Last Updated on STN: 19991202

AB Nonsteroidal anti-inflammatory drugs (NSAIDs) inhibit both cyclooxygenase (COX)-1 and COX-2 isoenzymes and are effective in the treatment of inflammatory disorders. This 8-week, double-masked, placebo- controlled trial was undertaken to assess the safety profile, tolerability, and effective dose range of once-daily **rofecoxib**, a COX-2-specific inhibitor, in the treatment of rheumatoid arthritis (RA). After a 3- to 15-day washout of prior NSAID therapy, 658 patients were randomly allocated to receive placebo or **rofecoxib** 5 mg, 25 mg, or 50 mg once daily. Safety profile, tolerability, and efficacy were evaluated after 2, 4, and 8 weeks of therapy. Six hundred fifty-eight patients (168, 158, 171, and 161 in the placebo and 5-mg, 25-mg, and 50-mg **rofecoxib** groups, respectively) were enrolled at 79 clinical centers in the United States. Mean age was 55 years, mean duration of RA was 10 years, and 506 (77%) of the 658 patients were female. All groups had similar baseline demographic characteristics. Patients taking **rofecoxib** 25 and 50 mg showed significant clinical improvement compared with those taking placebo; 43.9% in the **rofecoxib** 25-mg group and 49.7% in the **rofecoxib** 50-mg group completed the

treatment period and achieved an American College of Rheumatology 20 response (P = 0.025 and 0.001 vs placebo, respectively). The 5-mg dose of **rofecoxib** did not differ significantly from placebo. Patients in the **rofecoxib** 25- and 50-mg groups showed significant improvement in key individual efficacy measurements, including patient global assessment of pain, patient and investigator global assessment of disease activity, and Stanford Health Assessment Questionnaire Disability Index (P < 0.05 vs placebo). Compared with placebo, significantly fewer patients in the 25-mg and 50-mg **rofecoxib** groups discontinued therapy because of lack of efficacy (P = 0.02 and P = 0.032, respectively). Our results show that **rofecoxib** 25 and 50 mg once daily was effective and generally well-tolerated in patients with RA.

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ACCESSION NUMBER: 1999381366 EMBASE
TITLE: Understanding xenical and vioxx.
AUTHOR: Sisca T.
SOURCE: American Druggist, (**1999**) Vol. 216, No. 10, pp. 52-55.
ISSN: 0190-5279 CODEN: AMDRAG
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 006 Internal Medicine
010 Obstetrics and Gynecology
031 Arthritis and Rheumatism
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
ENTRY DATE: Entered STN: 19991118
Last Updated on STN: 19991118

DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L47 ANSWER 32 OF 44 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 1999380537 EMBASE
TITLE: A strategy for evaluating the novel COX-2 inhibitors versus NSAIDs for arthritis.
AUTHOR: Motheral B.R.; Bataoel J.R.; Armstrong E.P.
CORPORATE SOURCE: E.P. Armstrong, Department of Pharmacy Practice, College of Pharmacy, University of Arizona, Tucson, AZ, United States
SOURCE: Formulary, (**1999**) Vol. 34, No. 10, pp. 855-863.
Refs: 25
ISSN: 1082-801X CODEN: FORMF
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 030 Pharmacology
031 Arthritis and Rheumatism
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19991118
Last Updated on STN: 19991118

AB With the availability of the two new COX-2 inhibitors **celecoxib** and **rofecoxib**, drug decision makers must determine whether and how to cover them under the pharmacy benefit. The higher cost and improved side effect profile of the new COX-2 inhibitors must be weighed

against the lower cost and equivalent efficacy of the traditional NSAIDs. In this month's column, the authors demonstrate how to develop relevant pharmacoeconomic information to guide drug coverage decisions for these products.

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ACCESSION NUMBER: 1999377312 EMBASE
TITLE: Stomach and duodenum.
AUTHOR: Schubert M.L.
CORPORATE SOURCE: Dr. M.L. Schubert, McGuire VAMC, Code 111N, Gastroenterology Division, 1201 Broad Rock Boulevard, Richmond, VA 23249, United States. Mitchell.Schubert@med.va.gov
SOURCE: Current Opinion in Gastroenterology, (**1999**) Vol. 15, No. 6, pp. 455-456.
Refs: 3
ISSN: 0267-1379 CODEN: COGAEK
COUNTRY: United States
DOCUMENT TYPE: Journal; Editorial
FILE SEGMENT: 037 Drug Literature Index
048 Gastroenterology
LANGUAGE: English
ENTRY DATE: Entered STN: 19991118
Last Updated on STN: 19991118
DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L47 ANSWER 34 OF 44 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 1999347104 EMBASE
TITLE: Cyclooxygenase 2 selective inhibitors: Panacea or flash in the pan?.
AUTHOR: Beejay U.; Wolfe M.M.
CORPORATE SOURCE: Dr. M.M. Wolfe, Section of Gastroenterology, Boston Medical Center, 88 East Newton Street, Boston, MA 02118-2393, United States. michael.wolfe@bmc.org
SOURCE: Gastroenterology, (**1999**) Vol. 117, No. 4, pp. 1002-1005.
Refs: 34
ISSN: 0016-5085 CODEN: GASTAB
COUNTRY: United States
DOCUMENT TYPE: Journal; Editorial
FILE SEGMENT: 031 Arthritis and Rheumatism
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
LANGUAGE: English
ENTRY DATE: Entered STN: 19991021
Last Updated on STN: 19991021
DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L47 ANSWER 35 OF 44 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 1999333563 EMBASE
TITLE: [New aspects of treatment and prophylaxis of gastrointestinal side effects caused by nonsteroidal-antiinflammatory drugs (NSAIDs)]. NEUE ASPEKTE IN BEHANDLUNG UND PROPHYLAXE GASTROINTESTINALER NEBENWIRKUNGEN DURCH NICHT-STEROIDALE

ANTIPHLOGISTIKA (NSA).
AUTHOR: Braun J.; Sieper J.
CORPORATE SOURCE: Dr. J. Braun, Abt. fur Nephrologie/Endokrinologie, Universitatsklin. Benjamin Franklin, Freie Universitat Berlin, Hindenburgdamm 30, D-12200 Berlin, Germany. jbraun@zedat.fu-berlin.de
SOURCE: Zeitschrift fur Rheumatologie, (**1999**) Vol. 58, No. 4, pp. 173-184.
Refs: 52
ISSN: 0340-1855 CODEN: ZRHMBQ
COUNTRY: Germany
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 031 Arthritis and Rheumatism
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
LANGUAGE: German
SUMMARY LANGUAGE: English; German
ENTRY DATE: Entered STN: 19991017
Last Updated on STN: 19991017

AB Gastropathies caused by treatment with non-steroidal-antiinflammatory drugs (NSAIDs) are a frequent problem in rheumatology. An increased risk for this complication has been established for patients older than 70 years, for those with a history of ulcer and those under concomittant steroid medication. Especially those patients should be treated with gastroprotective drugs. In differing intensity, protone pump inhibitors, prostaglandine analoga and H2 blockers are able to prevent such problems and give some symptomatic relief. Most complications can be prevented using omeprazol, the newest and most expensive drug, in a dosage of 20 mg/day, a higher dosage is not more effective. This drug works also in many cases when the NSAID therapy has to be continued. A significant effect on the prevalence of serious GI effects was only shown for misoprostol in a dosage of 800 μg/day to date. Some influence on the risk for GI events can also be taken by questioning the indication, choice of the NSAD and proper information of the patient. The development of COX-2-selective and even specific NSAIDs might solve some of these drug related GI problems in the near future.

L47 ANSWER 36 OF 44 EMBASE
on STN
ACCESSION NUMBER: 1999297546 EMBASE
TITLE: [New perspectives in rheumatology: Specific COX-2 inhibitors]:
NOUVELLES PERSPECTIVES EN RHUMATOLOGIE: LES INHIBITEURS SPECIFIQUES COX- 2.
AUTHOR: Saudan-Kister A.
CORPORATE SOURCE: Dr. A. Saudan-Kister, Division de Rhumatologie, Hopital Cantonal Universitaire, 1211 Geneve 14, Switzerland
SOURCE: Medecine et Hygiene, (**4 Aug 1999**) Vol. 57, No. 2264, pp. 1506-1508.
Refs: 5
ISSN: 0025-6749 CODEN: MEHGAB
COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 030 Pharmacology
031 Arthritis and Rheumatism
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: French

ENTRY DATE: Entered STN: 19990910
Last Updated on STN: 19990910
DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L47 ANSWER 37 OF 44 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 1999254380 EMBASE
TITLE: **Rofecoxib** for osteoarthritis and pain.
SOURCE: Medical Letter on Drugs and Therapeutics, (**2 Jul 1999**) Vol. 41, No. 1056, pp. 59-61.
ISSN: 0025-732X CODEN: MELEAP
COUNTRY: United States
DOCUMENT TYPE: Journal; (Short Survey)
FILE SEGMENT: 031 Arthritis and Rheumatism
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
ENTRY DATE: Entered STN: 19990805
Last Updated on STN: 19990805
DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L47 ANSWER 38 OF 44 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 1999230828 EMBASE
TITLE: Reduction in morbidity and mortality associated with gastrointestinal bleeding in the elderly.
AUTHOR: Williams C.N.
CORPORATE SOURCE: Dr. C.N. Williams, Dalhousie University, Halifax, NS, Canada
SOURCE: Canadian Journal of Gastroenterology, (**1999**) Vol. 13, No. 5, pp. 375-376.
Refs: 19
ISSN: 0835-7900 CODEN: CJGAEJ
COUNTRY: Canada
DOCUMENT TYPE: Journal; (Short Survey)
FILE SEGMENT: 016 Cancer
030 Pharmacology
031 Arthritis and Rheumatism
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
LANGUAGE: English
ENTRY DATE: Entered STN: 19990715
Last Updated on STN: 19990715
DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L47 ANSWER 39 OF 44 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 1999230693 EMBASE
TITLE: Update on clinical developments with **celecoxib**, a new specific COX-2 inhibitor: What can we expect?.
AUTHOR: Geis G.S.
CORPORATE SOURCE: G.S. Geis, G. D. Searle and Co., 4901 Searle Parkway, Skokie, IL 60077, United States
SOURCE: Scandinavian Journal of Rheumatology, Supplement, (**1999**) Vol. 28, No. 109, pp. 31-37.
Refs: 19

ISSN: 0301-3847 CODEN: SJRSAS
COUNTRY: Norway
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 031 Arthritis and Rheumatism
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19990715
Last Updated on STN: 19990715

AB Nonsteroidal anti-inflammatory drugs (NSAIDs) are effective for the relief of pain and inflammation, yet their use is tempered by the development of side effects, primarily in the gastrointestinal (GI) tract. It is now known that inhibition of the enzyme cyclooxygenase (COX) is the principal mechanism for both the efficacy and the toxicity of NSAIDs. Recent research has shown that COX exists as at least two isoenzymes, COX-1 and COX-2. Compelling evidence suggests that COX-1 synthesizes prostaglandins that are involved in the regulation of normal cell activity (including GI cytoprotection), whereas COX-2 appears to produce prostaglandins mainly at sites of inflammation. These findings led to the search for compounds that would inhibit COX-2 without affecting COX-1. Several agents are under investigation in this new therapeutic category, including **celecoxib** (SC-58635). **Celecoxib** was developed as an anti-inflammatory and analgesic agent, and has been studied in preclinical studies and in clinical trials. This paper focuses on the results of five key clinical trials of **celecoxib**: an efficacy trial in dental pain, a 2-week osteoarthritis (OA) efficacy trial, a 4-week rheumatoid arthritis (RA) efficacy trial, a 1-week endoscopic study of GI mucosal effects, and a 10-day study of effects on platelet function. The arthritis trials identified **celecoxib** doses that were effective in treating OA and RA and that were distinguished from placebo on standard arthritis scales. In the upper GI endoscopy study, no ulcers occurred in subjects receiving **celecoxib** or placebo, whereas 19% of subjects receiving naproxen developed gastric ulcers. In the platelet effects trial, no statistically significant difference from placebo was seen in the effect of **celecoxib** on platelet aggregation or bleeding time. In contrast, naproxen caused statistically significant reductions in platelet aggregation and a statistically significant increase in bleeding time. These preliminary trials show that **celecoxib** achieves analgesic and anti-inflammatory efficacy in arthritis through specific COX-2 inhibition without showing evidence of two of the toxic effects of COX-1 inhibition associated with NSAIDs.

L47 ANSWER 40 OF 44 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 1999226798 EMBASE
TITLE: Second COX-2 inhibitor targeted for osteoarthritis, pain management.
SOURCE: Drug Topics, (**21 Jun 1999**) Vol. 143, No. 12, pp. 33-34.
ISSN: 0012-6616 CODEN: DGTNA7
COUNTRY: United States
DOCUMENT TYPE: Journal; (Short Survey)
FILE SEGMENT: 030 Pharmacology
031 Arthritis and Rheumatism
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English

ENTRY DATE: Entered STN: 19990715
Last Updated on STN: 19990715
DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L47 ANSWER 41 OF 44 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 1999206601 EMBASE
TITLE: Gastrointestinal toxicity of nonsteroidal antiinflammatory drugs.
AUTHOR: Wolfe M.M.; Lichtenstein D.R.; Singh G.
CORPORATE SOURCE: Dr. M.M. Wolfe, Boston Medical Center, Section of Gastroenterology, 88 E. Newton St., Boston, MA 02118-2393, United States. michael.wolfe@bmc.org
SOURCE: New England Journal of Medicine, (**17 Jun 1999**) Vol. 340, No. 24, pp. 1888-1899.
Refs: 113
ISSN: 0028-4793 CODEN: NEJMAG
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
LANGUAGE: English
ENTRY DATE: Entered STN: 19990701
Last Updated on STN: 19990701
DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L47 ANSWER 42 OF 44 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 1999111062 EMBASE
TITLE: Quarterly drug-approval update: Hits and misses.
AUTHOR: Goldenberg M.M.
CORPORATE SOURCE: Dr. M.M. Goldenberg, Mount Sinai NYU Health, New York, United States
SOURCE: P and T, (**1999**) Vol. 24, No. 3, pp. 129-132+135.
ISSN: 1052-1372 CODEN: PPTTEK
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
ENTRY DATE: Entered STN: 19990422
Last Updated on STN: 19990422
DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L47 ANSWER 43 OF 44 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 1998338083 EMBASE
TITLE: Preliminary study of the safety and efficacy of SC-58635, a novel cyclooxygenase 2 inhibitor. Efficacy and safety in two placebo-controlled trials in osteoarthritis and rheumatoid arthritis, and studies of gastrointestinal and platelet effects.
AUTHOR: Simon L.S.; Lanza F.L.; Lipsky P.E.; Hubbard R.C.; Talwalker S.; Schwartz B.D.; Isakson P.C.; Geis G.S.
CORPORATE SOURCE: Dr. L.S. Simon, Rheumatology/Metab. Bone Dis. Div., Beth Israel Deaconess Medical Center, Lowry Medical Office Building, 110 Francis Street, Boston, MA 02215, United

States
SOURCE: Arthritis and Rheumatism, (**1998**) Vol. 41, No. 9, pp. 1591-1602.
Refs: 56
ISSN: 0004-3591 CODEN: ARHEAW
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 031 Arthritis and Rheumatism
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19981028
Last Updated on STN: 19981028

AB Objective. To investigate the efficacy and safety of SC-58635 (**celecoxib**), an antiinflammatory and analgesic agent that acts by selective cyclooxygenase 2 (COX-2) inhibition and is not expected to cause the typical gastrointestinal (GI), renal, and platelet-related side effects associated with inhibition of the COX-1 enzyme. Methods. Four phase II trials were performed: a 2-week osteoarthritis efficacy trial, a 4-week rheumatoid arthritis efficacy trial, a 1-week endoscopic study of GI mucosal effects, and a 1-week study of effects on platelet function. Results. The 2 arthritis trials identified: SC-58635 dosage levels that were consistently effective in treating the signs and symptoms of arthritis and were distinguished from placebo on standard arthritis scales. In the upper GI endoscopy study, 19% of subjects receiving naproxen (6 of 32) developed gastric ulcers, whereas no ulcers occurred in subjects receiving SC-58635 or placebo. The study of platelet effects revealed no meaningful effect of SC-58635 on platelet aggregation or thromboxane B2 levels, whereas aspirin caused significant decreases in 2 of 3 platelet aggregation measures and thromboxane B2 levels. In all 4 trials, SC-58635 was well tolerated, with a safety profile similar to that of placebo. Conclusion. SC-58635 achieves analgesic and antiinflammatory efficacy in arthritis through selective COX-2 inhibition, without showing any evidence of 2 of the toxic effects of COX-1 inhibition associated with nonsteroidal antiinflammatory drugs.

L47 ANSWER 44 OF 44 EMBASE
on STN
ACCESSION NUMBER: 97106111 EMBASE
DOCUMENT NUMBER: 1997106111
TITLE: [Selective cyclooxygenase 2 (COX-2) inhibitors - Progress in the treatment of rheumatic diseases?].
SELEKTIVE CYCLOOXYGENASE-2 (COX-2)-HEMMER. FORTSCHRITT IN DER RHEUMABEHANDLUNG?.
AUTHOR: Reuss-Borst M.
CORPORATE SOURCE: Dr. M. Reuss-Borst, Abtlg. Nephrologie/Rheumatologie, Universitatsklinik Gottingen, Robert-Koch-Str. 40, D-37075 Gottingen, Germany
SOURCE: Internist, (**1997**) Vol. 38, No. 3, pp. 266-271.
Refs: 35
ISSN: 0020-9554 CODEN: INTEAG
COUNTRY: Germany
DOCUMENT TYPE: Journal; (Short Survey)
FILE SEGMENT: 006 Internal Medicine
031 Arthritis and Rheumatism
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles

LANGUAGE: German
ENTRY DATE: Entered STN: 970520
Last Updated on STN: 970520
DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

Inventor Search

=> d ibib abs hitstr l23 1-2

L23 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:581708 HCAPLUS
DOCUMENT NUMBER: 135:147440
TITLE: Use of cyclooxygenase-2 (COX-2) inhibitors as gastroprokinetic agents
INVENTOR(S): **Mangel, Allen Wayne; Naylor, Alan**
PATENT ASSIGNEE(S): GlaxoSmithKline, UK
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

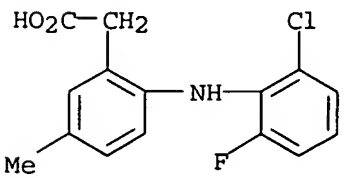
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001056573	A1	20010809	WO 2001-GB423	20010201
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001030395	A5	20010814	AU 2001-30395	20010201
EP 1259239	A2	20021127	EP 2001-902541	20010201
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003521516	T2	20030715	JP 2001-556472	20010201
US 2003022897	A1	20030130	US 2002-182080	20020725
US 6759413	B2	20040706		
US 2004192694	A1	20040930	US 2004-786423	20040225

PRIORITY APPLN. INFO.:		
GB 2000-2336	A	20000201
WO 2001-GB423	W	20010201
US 2002-182080	A1	20020725

AB The invention provides a COX-2 inhibitor or a pharmaceutically acceptable derivative thereof for use in the treatment of a disorder ameliorated by a gastroprokinetic agent.

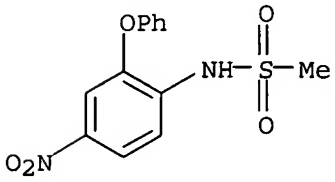
IT **220991-20-8**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(COX 189; cyclooxygenase-2 inhibitors as gastroprokinetic agents)

RN 220991-20-8 HCAPLUS
CN Benzeneacetic acid, 2-[(2-chloro-6-fluorophenyl)amino]-5-methyl- (9CI) (CA INDEX NAME)

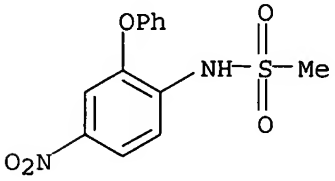


IT **51803-78-2**, Nimesulide **51803-78-2D**, Nimesulide, derivs.
80937-31-1, Flosulide **80937-31-1D**, Flosulide, derivs.
81098-60-4, Cisapride **123653-11-2**, NS 398
123653-11-2D, NS 398, derivs. **158205-05-1**, L-745337
158205-05-1D, L-745337, derivs. **162011-90-7**, Rofecoxib
162011-90-7D, Rofecoxib, derivs. **169590-42-5**, Celecoxib
169590-42-5D, Celecoxib, derivs. **180200-68-4**, JTE-522
180200-68-4D, JTE-522, derivs. **181695-72-7**, Valdecoxib
181695-72-7D, Valdecoxib, derivs. **183610-65-3**
183610-65-3D, derivs. **189954-66-3** **189954-66-3D**
, derivs. **198470-84-7**, Parecoxib **198470-84-7D**,
Parecoxib, derivs. **202409-33-4**, Etoricoxib **202409-33-4D**
, Etoricoxib, derivs. **220991-20-8D**, derivs. **221148-46-5**
221148-46-5D, derivs. **267235-56-3** **267235-56-3D**
, derivs. **342651-37-0** **342651-37-0D**, derivs.
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclooxygenase-2 inhibitors as gastroprokinetic agents)

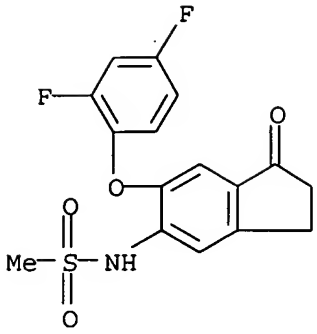
RN 51803-78-2 HCAPLUS
CN Methanesulfonamide, N-(4-nitro-2-phenoxyphenyl)- (9CI) (CA INDEX NAME)



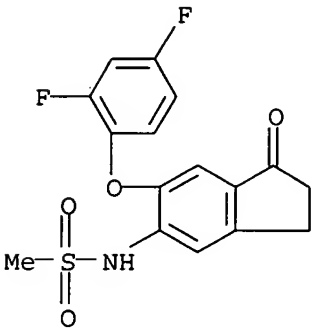
RN 51803-78-2 HCAPLUS
CN Methanesulfonamide, N-(4-nitro-2-phenoxyphenyl)- (9CI) (CA INDEX NAME)



RN 80937-31-1 HCAPLUS
CN Methanesulfonamide, N-[6-(2,4-difluorophenoxy)-2,3-dihydro-1-oxo-1H-inden-5-yl]- (9CI) (CA INDEX NAME)

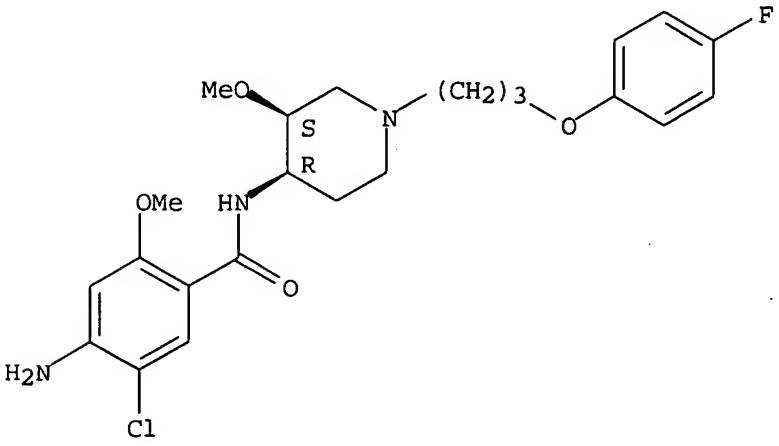


RN 80937-31-1 HCAPLUS
CN Methanesulfonamide, N-[6-(2,4-difluorophenoxy)-2,3-dihydro-1-oxo-1H-inden-5-yl]- (9CI) (CA INDEX NAME)



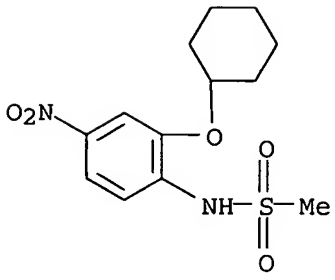
RN 81098-60-4 HCAPLUS
CN Benzamide, 4-amino-5-chloro-N-[1-[(3R,4S)-3-(4-fluorophenoxy)propyl]-3-methoxy-4-piperidinyl]-2-methoxy-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

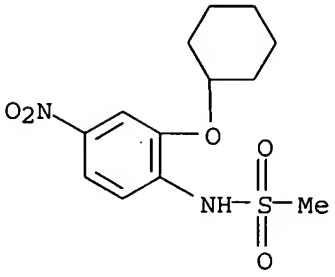


RN 123653-11-2 HCAPLUS

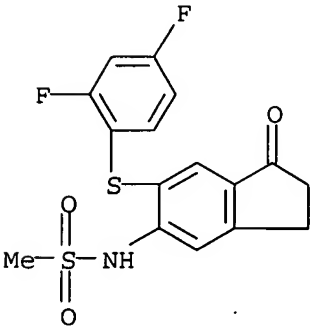
CN Methanesulfonamide, N-[2-(cyclohexyloxy)-4-nitrophenyl]- (9CI) (CA INDEX NAME)



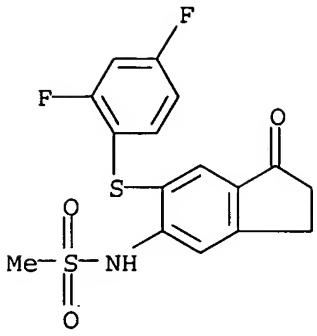
RN 123653-11-2 HCAPLUS
CN Methanesulfonamide, N-[2-(cyclohexyloxy)-4-nitrophenyl]- (9CI) (CA INDEX NAME)



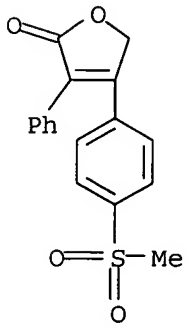
RN 158205-05-1 HCAPLUS
CN Methanesulfonamide, N-[6-[(2,4-difluorophenyl)thio]-2,3-dihydro-1-oxo-1H-inden-5-yl]- (9CI) (CA INDEX NAME)



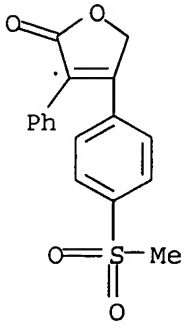
RN 158205-05-1 HCAPLUS
CN Methanesulfonamide, N-[6-[(2,4-difluorophenyl)thio]-2,3-dihydro-1-oxo-1H-inden-5-yl]- (9CI) (CA INDEX NAME)



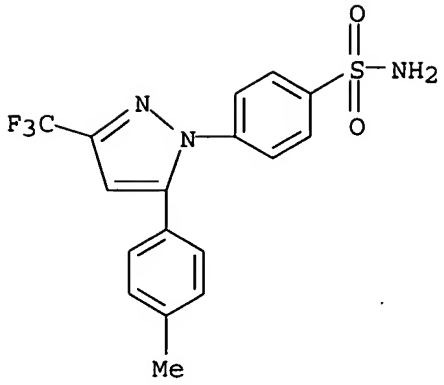
RN 162011-90-7 HCAPLUS
CN 2(5H)-Furanone, 4-[4-(methylsulfonyl)phenyl]-3-phenyl- (9CI) (CA INDEX NAME)



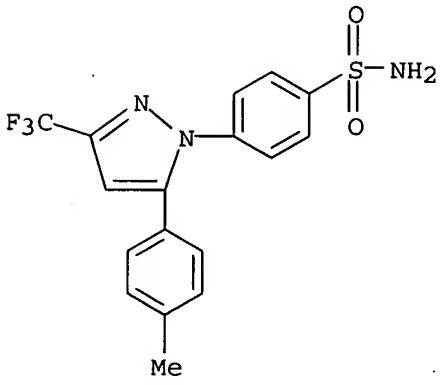
RN 162011-90-7 HCAPLUS
CN 2(5H)-Furanone, 4-[4-(methylsulfonyl)phenyl]-3-phenyl- (9CI) (CA INDEX NAME)



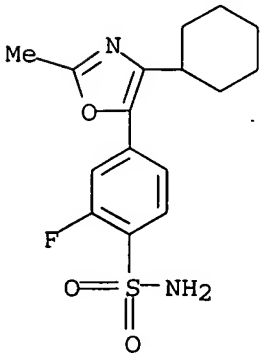
RN 169590-42-5 HCAPLUS
CN Benzenesulfonamide, 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



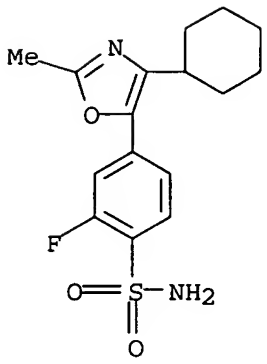
RN 169590-42-5 HCAPLUS
CN Benzenesulfonamide, 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



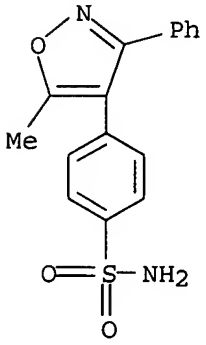
RN 180200-68-4 HCAPLUS
CN Benzenesulfonamide, 4-(4-cyclohexyl-2-methyl-5-oxazolyl)-2-fluoro- (9CI) (CA INDEX NAME)



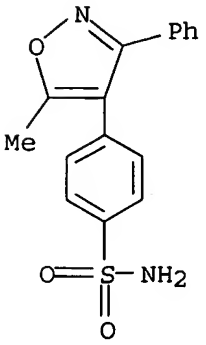
RN 180200-68-4 HCAPLUS
CN Benzenesulfonamide, 4-(4-cyclohexyl-2-methyl-5-oxazolyl)-2-fluoro- (9CI) (CA INDEX NAME)



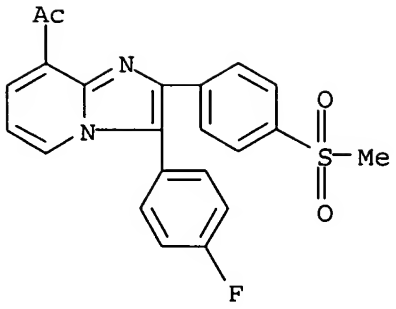
RN 181695-72-7 HCAPLUS
CN Benzenesulfonamide, 4-(5-methyl-3-phenyl-4-isoxazolyl)- (9CI) (CA INDEX NAME)



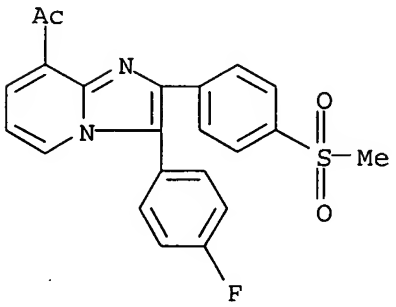
RN 181695-72-7 HCAPLUS
CN Benzenesulfonamide, 4-(5-methyl-3-phenyl-4-isoxazolyl)- (9CI) (CA INDEX NAME)



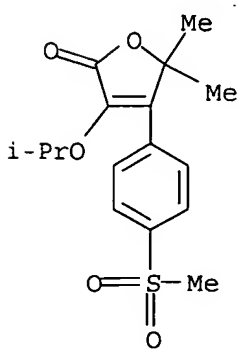
RN 183610-65-3 HCAPLUS
CN Ethanone, 1-[3-(4-fluorophenyl)-2-[4-(methylsulfonyl)phenyl]imidazo[1,2-a]pyridin-8-yl]- (9CI) (CA INDEX NAME)



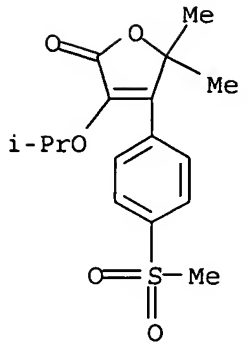
RN 183610-65-3 HCAPLUS
CN Ethanone, 1-[3-(4-fluorophenyl)-2-[4-(methylsulfonyl)phenyl]imidazo[1,2-a]pyridin-8-yl]- (9CI) (CA INDEX NAME)



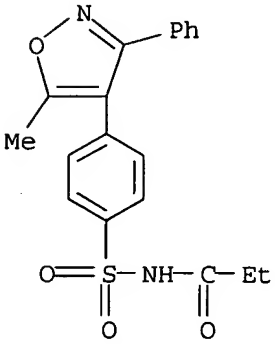
RN 189954-66-3 HCAPLUS
CN 2(5H)-Furanone, 5,5-dimethyl-3-(1-methylethoxy)-4-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



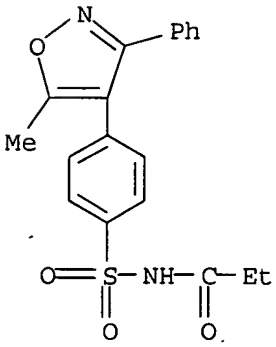
RN 189954-66-3 HCAPLUS
CN 2(5H)-Furanone, 5,5-dimethyl-3-(1-methylethoxy)-4-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



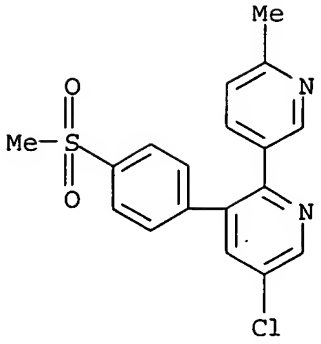
RN 198470-84-7 HCAPLUS
CN Propanamide, N-[[4-(5-methyl-3-phenyl-4-isoxazolyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)



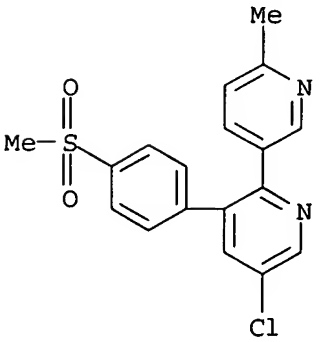
RN 198470-84-7 HCAPLUS
CN Propanamide, N-[[4-(5-methyl-3-phenyl-4-isoxazolyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)



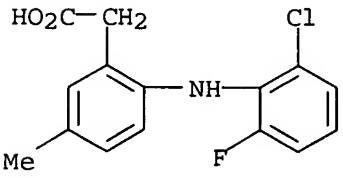
RN 202409-33-4 HCAPLUS
CN 2,3'-Bipyridine, 5-chloro-6'-methyl-3-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



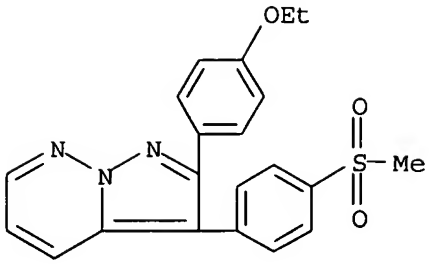
RN 202409-33-4 HCAPLUS
CN 2,3'-Bipyridine, 5-chloro-6'-methyl-3-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



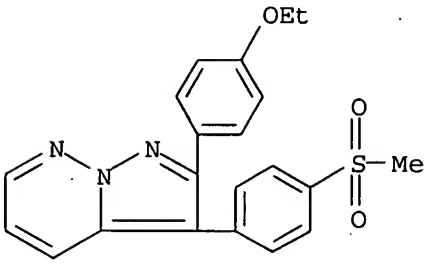
RN 220991-20-8 HCAPLUS
CN Benzeneacetic acid, 2-[(2-chloro-6-fluorophenyl)amino]-5-methyl- (9CI) (CA INDEX NAME)



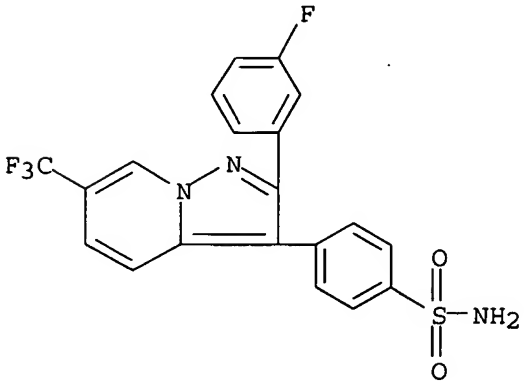
RN 221148-46-5 HCAPLUS
CN Pyrazolo[1,5-b]pyridazine, 2-(4-ethoxyphenyl)-3-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



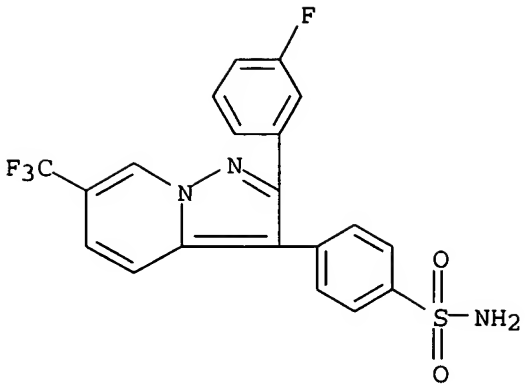
RN 221148-46-5 HCAPLUS
CN Pyrazolo[1,5-b]pyridazine, 2-(4-ethoxyphenyl)-3-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



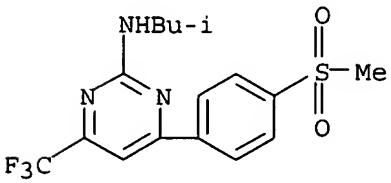
RN 267235-56-3 HCAPLUS
CN Benzenesulfonamide, 4-[2-(3-fluorophenyl)-6-(trifluoromethyl)pyrazolo[1,5-a]pyridin-3-yl]- (9CI) (CA INDEX NAME)



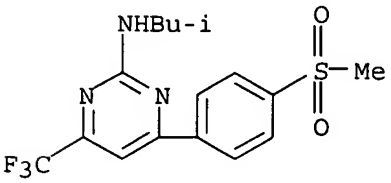
RN 267235-56-3 HCAPLUS
CN Benzenesulfonamide, 4-[2-(3-fluorophenyl)-6-(trifluoromethyl)pyrazolo[1,5-a]pyridin-3-yl]- (9CI) (CA INDEX NAME)



RN 342651-37-0 HCAPLUS
CN 2-Pyrimidinamine, N-(2-methylpropyl)-4-[4-(methylsulfonyl)phenyl]-6-(trifluoromethyl)- (9CI) (CA INDEX NAME)



RN 342651-37-0 HCAPLUS
CN 2-Pyrimidinamine, N-(2-methylpropyl)-4-[4-(methylsulfonyl)phenyl]-6-(trifluoromethyl)- (9CI) (CA INDEX NAME)



IT **329967-85-3**, Cyclooxygenase 1
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(cyclooxygenase-2 inhibitors as gastroprokinetic agents)
RN 329967-85-3 HCAPLUS
CN Synthetase, prostaglandin endoperoxide, 1 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **329900-75-6**, Cyclooxygenase 2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cyclooxygenase-2 inhibitors as gastroprokinetic agents)
RN 329900-75-6 HCAPLUS
CN Synthetase, prostaglandin endoperoxide, 2 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

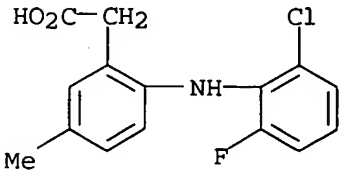
L23 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:581693 HCAPLUS
DOCUMENT NUMBER: 135:147439
TITLE: Use of cyclooxygenase-2 (COX-2) inhibitors for constipation
INVENTOR(S): **Mangel, Allen Wayne; Naylor, Alan**
PATENT ASSIGNEE(S): Glaxo Group Limited, UK
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001056555	A2	20010809	WO 2001-GB416	20010201
WO 2001056555	A3	20020808		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1251839	A2	20021030	EP 2001-948935	20010201
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003521511	T2	20030715	JP 2001-556247	20010201
US 2003013717	A1	20030116	US 2002-182169	20020725
PRIORITY APPLN. INFO.:			GB 2000-2312 A	20000201
			WO 2001-GB416 W	20010201

AB The invention provides a COX-2 inhibitor or a pharmaceutically acceptable derivative thereof for use in the treatment of constipation.

IT **220991-20-8**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(COX 189; cyclooxygenase-2 inhibitors for treatment of constipation)

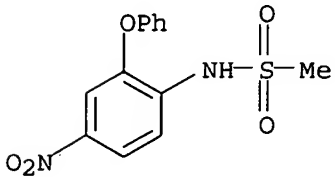
RN 220991-20-8 HCAPLUS
CN Benzeneacetic acid, 2-[(2-chloro-6-fluorophenyl)amino]-5-methyl- (9CI) (CA INDEX NAME)



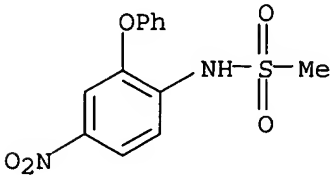
IT **51803-78-2**, Nimesulide **51803-78-2D**, Nimesulide, derivs.
80937-31-1, Flosulide **80937-31-1D**, Flosulide, derivs.
81098-60-4, Cisapride **123653-11-2**, NS 398
123653-11-2D, NS 398, derivs. **158205-05-1**, L-745337

158205-05-1D, L-745337, derivs. **162011-90-7**, Rofecoxib
162011-90-7D, Rofecoxib, derivs. **169590-42-5**, Celecoxib
169590-42-5D, Celecoxib, derivs. **180200-68-4**, JTE-522
180200-68-4D, JTE-522, derivs. **181695-72-7**, Valdecoxib
181695-72-7D, Valdecoxib, derivs. **183610-65-3**
183610-65-3D, derivs. **189954-66-3 189954-66-3D**
, derivs. **198470-84-7**, Parecoxib **198470-84-7D**,
Parecoxib, derivs. **202409-33-4**, Etoricoxib **202409-33-4D**
, Etoricoxib, derivs. **220991-20-8D**, derivs. **221148-46-5**
221148-46-5D, derivs. **267235-56-3 267235-56-3D**
, derivs. **342651-37-0 342651-37-0D**, derivs.
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclooxygenase-2 inhibitors for treatment of constipation)

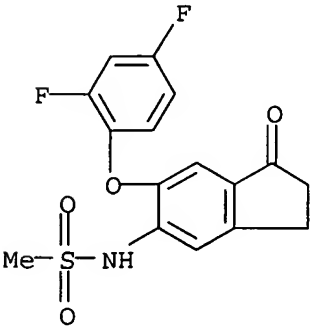
RN 51803-78-2 HCAPLUS
CN Methanesulfonamide, N-(4-nitro-2-phenoxyphenyl)- (9CI) (CA INDEX NAME)



RN 51803-78-2 HCAPLUS
CN Methanesulfonamide, N-(4-nitro-2-phenoxyphenyl)- (9CI) (CA INDEX NAME)

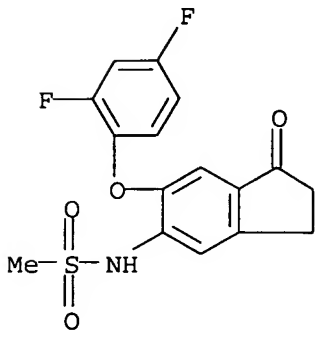


RN 80937-31-1 HCAPLUS
CN Methanesulfonamide, N-[6-(2,4-difluorophenoxy)-2,3-dihydro-1-oxo-1H-inden-5-yl]- (9CI) (CA INDEX NAME)



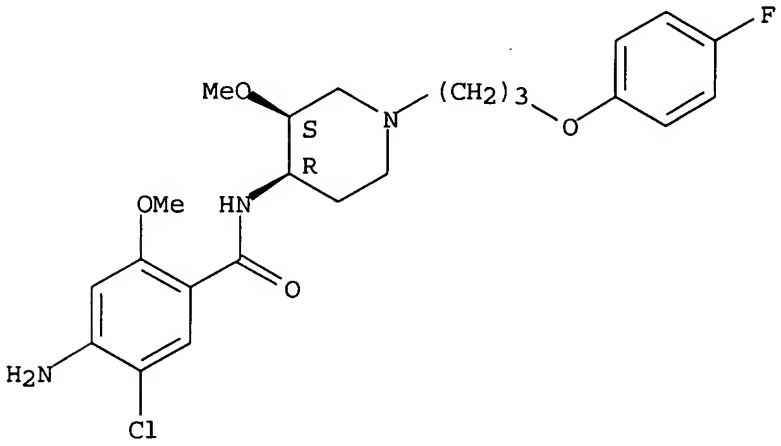
RN 80937-31-1 HCAPLUS

CN Methanesulfonamide, N-[6-(2,4-difluorophenoxy)-2,3-dihydro-1-oxo-1H-inden-5-yl]- (9CI) (CA INDEX NAME)

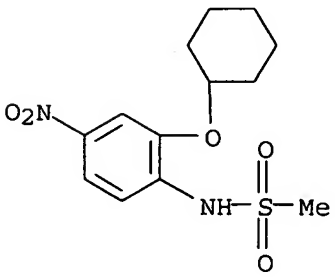


RN 81098-60-4 HCAPLUS
CN Benzamide, 4-amino-5-chloro-N-[1-[(3R,4S)-3-(4-fluorophenoxy)propyl]-3-methoxy-4-piperidinyl]-2-methoxy-, rel- (9CI) (CA INDEX NAME)

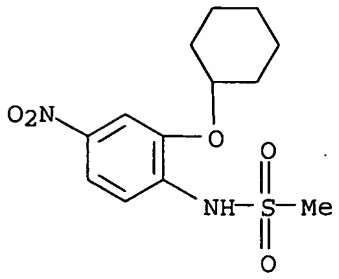
Relative stereochemistry.



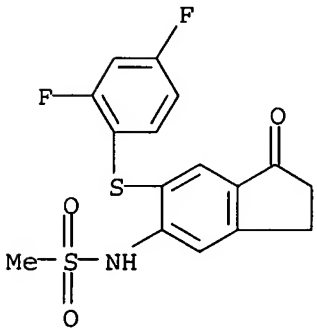
RN 123653-11-2 HCAPLUS
CN Methanesulfonamide, N-[2-(cyclohexyloxy)-4-nitrophenyl]- (9CI) (CA INDEX NAME)



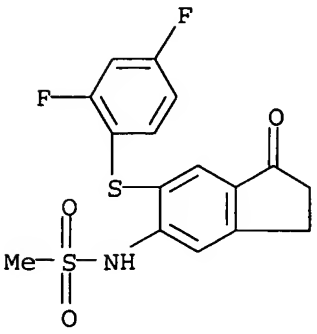
RN 123653-11-2 HCAPLUS
CN Methanesulfonamide, N-[2-(cyclohexyloxy)-4-nitrophenyl]- (9CI) (CA INDEX NAME)



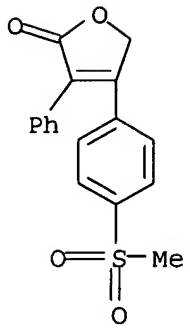
RN 158205-05-1 HCAPLUS
CN Methanesulfonamide, N-[6-[(2,4-difluorophenyl)thio]-2,3-dihydro-1-oxo-1H-inden-5-yl]- (9CI) (CA INDEX NAME)



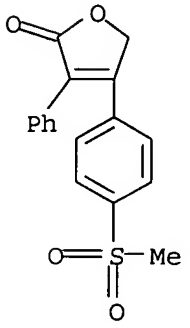
RN 158205-05-1 HCAPLUS
CN Methanesulfonamide, N-[6-[(2,4-difluorophenyl)thio]-2,3-dihydro-1-oxo-1H-inden-5-yl]- (9CI) (CA INDEX NAME)



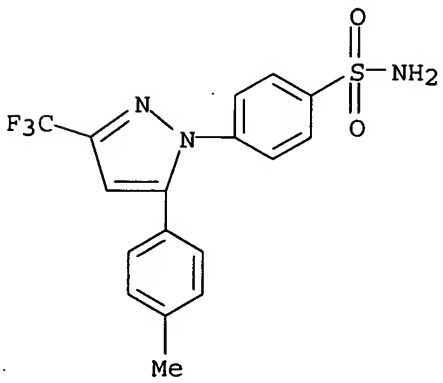
RN 162011-90-7 HCAPLUS
CN 2(5H)-Furanone, 4-[4-(methylsulfonyl)phenyl]-3-phenyl- (9CI) (CA INDEX NAME)



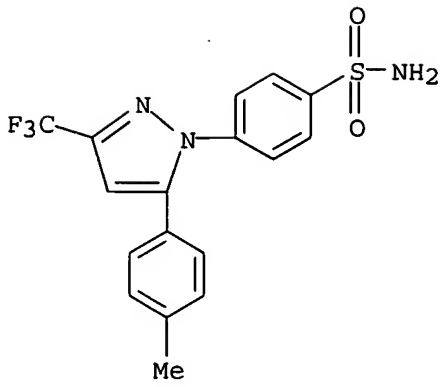
RN 162011-90-7 HCAPLUS
CN 2(5H)-Furanone, 4-[4-(methylsulfonyl)phenyl]-3-phenyl- (9CI) (CA INDEX NAME)



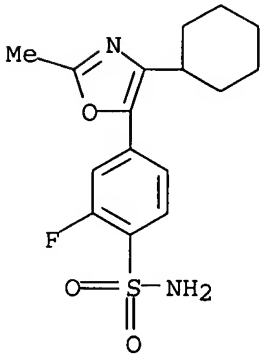
RN 169590-42-5 HCAPLUS
CN Benzenesulfonamide, 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



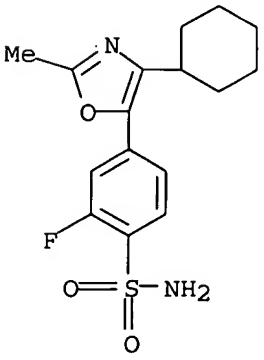
RN 169590-42-5 HCAPLUS
CN Benzenesulfonamide, 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



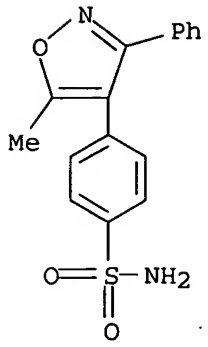
RN 180200-68-4 HCAPLUS
CN Benzenesulfonamide, 4-(4-cyclohexyl-2-methyl-5-oxazolyl)-2-fluoro- (9CI) (CA INDEX NAME)



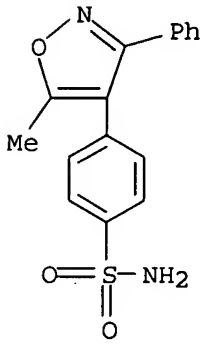
RN 180200-68-4 HCAPLUS
CN Benzenesulfonamide, 4-(4-cyclohexyl-2-methyl-5-oxazolyl)-2-fluoro- (9CI) (CA INDEX NAME)



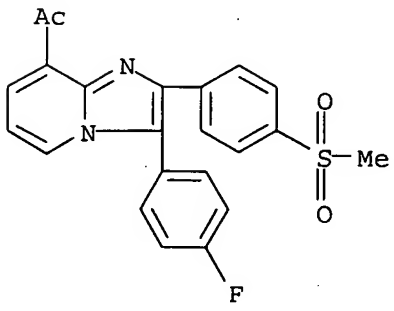
RN 181695-72-7 HCAPLUS
CN Benzenesulfonamide, 4-(5-methyl-3-phenyl-4-isoxazolyl)- (9CI) (CA INDEX NAME)



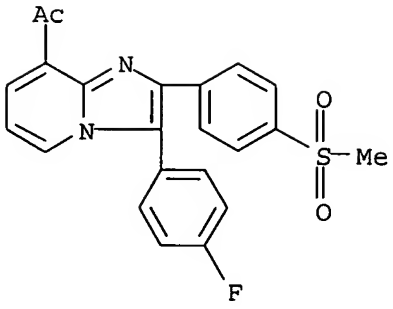
RN 181695-72-7 HCAPLUS
CN Benzenesulfonamide, 4-(5-methyl-3-phenyl-4-isoxazolyl)- (9CI) (CA INDEX NAME)



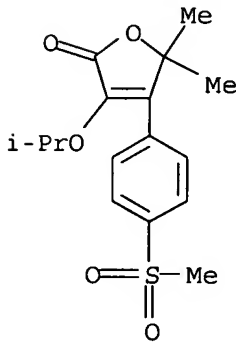
RN 183610-65-3 HCAPLUS
CN Ethanone, 1-[3-(4-fluorophenyl)-2-[4-(methylsulfonyl)phenyl]imidazo[1,2-a]pyridin-8-yl]- (9CI) (CA INDEX NAME)



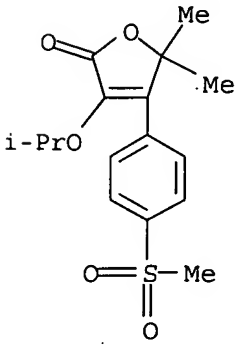
RN 183610-65-3 HCAPLUS
CN Ethanone, 1-[3-(4-fluorophenyl)-2-[4-(methylsulfonyl)phenyl]imidazo[1,2-a]pyridin-8-yl]- (9CI) (CA INDEX NAME)



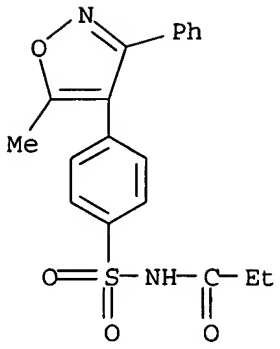
RN 189954-66-3 HCAPLUS
CN 2(5H)-Furanone, 5,5-dimethyl-3-(1-methylethoxy)-4-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



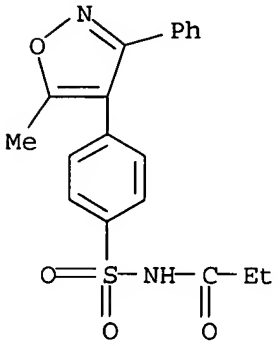
RN 189954-66-3 HCAPLUS
CN 2(5H)-Furanone, 5,5-dimethyl-3-(1-methylethoxy)-4-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



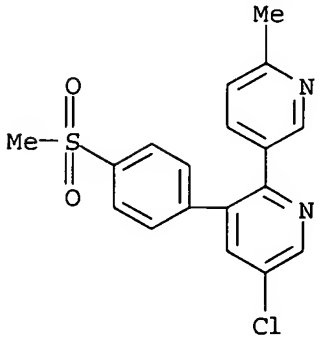
RN 198470-84-7 HCAPLUS
CN Propanamide, N-[[4-(5-methyl-3-phenyl-4-isoxazolyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)



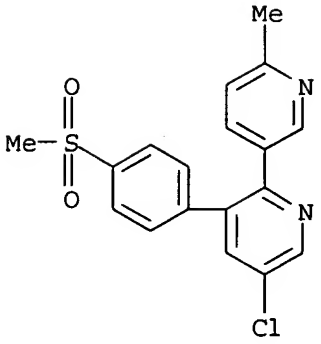
RN 198470-84-7 HCAPLUS
CN Propanamide, N-[[4-(5-methyl-3-phenyl-4-isoxazolyl)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)



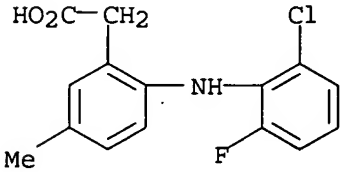
RN 202409-33-4 HCAPLUS
CN 2,3'-Bipyridine, 5-chloro-6'-methyl-3-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



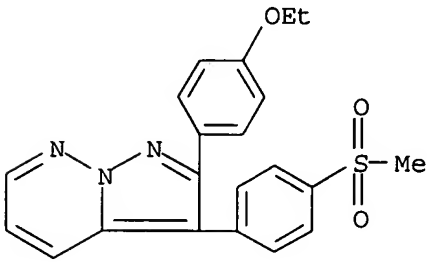
RN 202409-33-4 HCAPLUS
CN 2,3'-Bipyridine, 5-chloro-6'-methyl-3-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



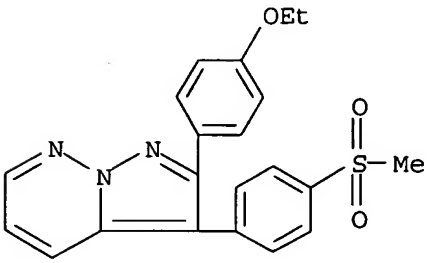
RN 220991-20-8 HCAPLUS
CN Benzeneacetic acid, 2-[(2-chloro-6-fluorophenyl)amino]-5-methyl- (9CI) (CA INDEX NAME)



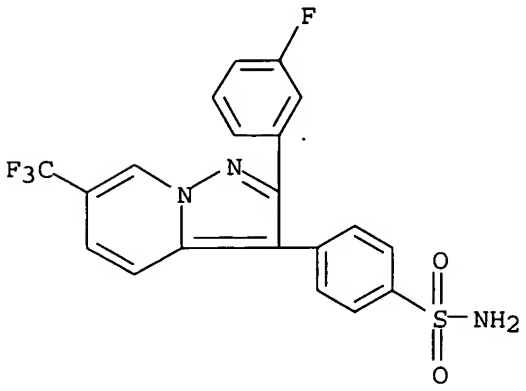
RN 221148-46-5 HCAPLUS
CN Pyrazolo[1,5-b]pyridazine, 2-(4-ethoxyphenyl)-3-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



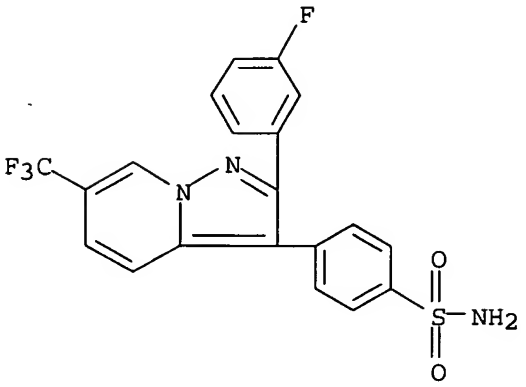
RN 221148-46-5 HCAPLUS
CN Pyrazolo[1,5-b]pyridazine, 2-(4-ethoxyphenyl)-3-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



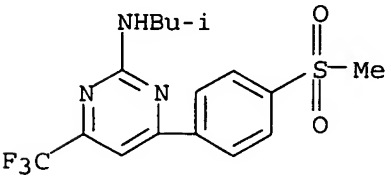
RN 267235-56-3 HCAPLUS
CN Benzenesulfonamide, 4-[2-(3-fluorophenyl)-6-(trifluoromethyl)pyrazolo[1,5-a]pyridin-3-yl]- (9CI) (CA INDEX NAME)



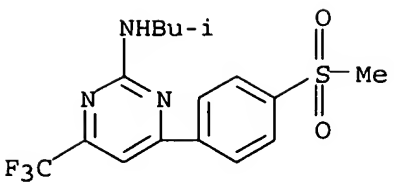
RN 267235-56-3 HCAPLUS
CN Benzenesulfonamide, 4-[2-(3-fluorophenyl)-6-(trifluoromethyl)pyrazolo[1,5-a]pyridin-3-yl]- (9CI) (CA INDEX NAME)



RN 342651-37-0 HCAPLUS
CN 2-Pyrimidinamine, N-(2-methylpropyl)-4-[4-(methylsulfonyl)phenyl]-6-(trifluoromethyl)- (9CI) (CA INDEX NAME)



RN 342651-37-0 HCAPLUS
CN 2-Pyrimidinamine, N-(2-methylpropyl)-4-[4-(methylsulfonyl)phenyl]-6-(trifluoromethyl)- (9CI) (CA INDEX NAME)



IT **329967-85-3**, Cyclooxygenase 1
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(cyclooxygenase-2 inhibitors for treatment of constipation)
RN 329967-85-3 HCAPLUS
CN Synthetase, prostaglandin endoperoxide, 1 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **329900-75-6**, Cyclooxygenase 2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cyclooxygenase-2 inhibitors for treatment of constipation)
RN 329900-75-6 HCAPLUS
CN Synthetase, prostaglandin endoperoxide, 2 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***